CLINICAL ROENTGENOLOGY OF THE DIGESTIVE TRACT

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Dedicated to my sons

MAURICE FELDMAN, JR., A.B., M.D.

and

CHARLES FELDMAN, A.B.

PREFACE OF THE THIRD EDITION

This book was written to present a clinical roentgenological consideration of the diseases of the gastrointestinal tract. It was written as an aid for the diagnosis of the digestive tract for the roentgenologist, gastroenterologist, student and general practitioner. The need for a book of this type is evidenced by the difficulty one encounters in seeking information on this subject. During the many years in which I have been interested in diagnostic roentgenology of the gastrointestinal tract, I have felt the need of bringing together sources of material which have not heretofore been compiled in a single volume. In collecting the necessary material I have endeavored to cover every phase of the gastrointestinal tract with the object in view of presenting the importance of the diagnostic value of the roentgen examination.

In assembling the material it has not been my intention to mention all of the authors who have contributed to the literature, but only those whose contributions were pertinent to the subject matter. Due credit has been given to each author quoted, and to any who have been inadvertently omitted I wish to express my regrets and credit is here given to them.

In the third edition changes have been made in order to bring the material up to date. Many new chapters, additional information and illustrations have been added.

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CHAPTER I

THE ESOPHAGUS

THE PHARYNGO-ESOPHAGUS

In the routine gastrointestinal roentgen examination the pharyngo-esophageal region is studied. The barium mixture usually passes through this segment rapidly while erect, but may be slowed if the examination is made in the recumbent position. The pharyngo-esophagus is best studied by means of the fluoroscope. If roentgenograms are to be made, the timing with the swallowing action must be carefully observed; otherwise, the segment will be emptied. The patient is given a mouthful of barium and is instructed to swallow, at which time the examination is made. The fluoroscopic examination is begun immediately before the swallowing action.

The caliber of the pharyngo-esophagus, the valleculae and pyriform sinuses, residues, asymmetries and spastic phenomena are noted. Functional disorders affecting the pharyngo-esophagus are common.

ESOPHAGUS

The esophagus is a collapsible, distensible musculo-membranous tube about 16 inches in length, beginning opposite the upper border of the cricoid cartilage about 6 inches beyond the incisor teeth and extending from the pharynx to the stomach. It enters the stomach slightly below the diaphragm. The abdominal portion varies in length from 1 to 4 centimeters. The general direction is vertical with three slight curves in its course. The esophagus begins in midline and deviates to the left as far as the root of the neck where it gradually returns toward the midline. In the lower end it again deviates to the left, passing forward to the esophageal orifice in the diaphragm. Its caliber varies slightly; usually it is about 2 centimeters in diameter. It is narrowest at its beginning and where it passes through the diaphragm. The phrenic ampulla is a localized dilatation of the lower end of the esophagus. This is a normal phenomenon commonly seen in the routine examination. Often it is associated with a cardio-esophageal spasm which narrows the opening and temporarily retards the flow of barium into the stomach.

The esophagus occupies the posterior mediastinum anterior to the loose tissue of the trachea. It lies to the right and passes in front of the aorta just before it enters the abdomen. The pleura are on either side and the pericardium is in front. Posteriorly it lies close to the vertebral column.

The esophagus is divided into three portions: the cervical, thoracic and abdominal. Four normal points of narrowing are observed: (1) level of





Fig 1 Fig 2

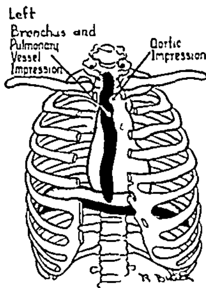
Fig 1 Normal filling of the pharyngo esophagus lateral view the normal upper esophagus
Fig 2 Antero posterior view showing the bulbous appearance of the pharyngoesophagus



Fig 3 Complete filling of the esophagus in a case of pyloric obstruction Arrows point to slight narrowing at the cardioesophageal juncture with an annular filling defect at the pylorus

the cricoid cartilage (2) crossing of the aorta, (3) crossing of the left bronchus, (4) at the cardia

Roentgen diagnosis The roentgen examination will demonstrate evidence of obstruction or delay in the passage of the opaque meal defects, contour irregularities displacement signs of pressure and spasm The examination begins with the swallowing of the first intake of the opaque meal and the mechanism is observed under the fluoroscope Normally one visualizes the rapid transit of barium through the upper portion of the esophagus by gravity and through the lower portion by peristaltic activity Before entering the stomach its passage is slowed Fluids descend in a continuous quick stream while semi solids travel slower and the column is usually broken The detection of peristalsis is difficult because of the



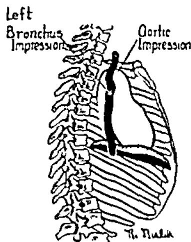


FIG 4 FIG 5

FIG 4 The normal esophagus antero-posterior view showing the aortic and pulmonary vessel impressions
FIG 5 Right oblique view showing the aortic and the left bronchus impression

rapidity with which the meal passes down the esophagus In the roentgen examination the patient is placed in an erect and recumbent position and is rotated obliquely or laterally The right recumbent prone position produces a slight upgrade of the esophagus The advantage of this position is that it slows the passage of the opaque meal and permits a detailed study Placing the patient in the Trendelenburg position will further retard the meal The small caliber of the lumen and the rapid transit of the meal afford a relief view of the esophagus The normal esophagus especially in the lower third shows several longitudinal parallel mucosal folds Inflammatory changes are evidenced by a marked widening of these mucosal folds The relief view will often disclose before any characteristic symptoms are

noted, the early signs of carcinoma, esophagitis, diverticula, peptic ulcer, varicosities and esophageal hernias

The fluoroscopic examination of the esophagus is the method of choice. Films are made while the patient is drinking the opaque meal so that the filling of the entire esophagus may be demonstrated. Normally, the lumen is well outlined and its contour is usually smooth. The flow of barium is carefully watched, particularly as it approaches the cardia and enters the

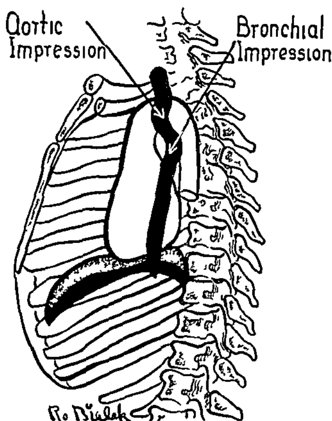


FIG 6 Left oblique view of esophagus, the aortic and bronchial impression are shown

stomach. To demonstrate the lower end of the esophagus the patient is instructed to take deep breaths immediately after swallowing a mouthful of the barium. This procedure temporarily retards the meal at the cardia. The administration of a thick barium paste is often indicated to study the esophagus. A bismuth filled 00 capsule may be given to determine the descent of solids.

The thickness of the barium meal depends upon the type of examination

to be made For relief views a thick barium is used for the demonstration of varices a thin barium mixture is employed The rapid descent of the opaque meal makes it necessary to employ short exposures $\frac{1}{10}$–$\frac{3}{10}$ seconds, in order to obtain a roentgenogram of the upper esophagus

CLASSIFICATION OF CONGENITAL ANOMALIES OF THE ESOPHAGUS

Congenital anomalies of the esophagus are classified as (1) absence of the entire esophagus (2) entire esophagus represented by a solid cord, (3) double esophagus a complete doubling of its entire length b partial doubling of a short segment c bifurcation with reunion at the lower end (4) atresia with a simple cul-de-sac, (5) atresia with a solid cord between both ends without fistulous communication, (6) atresia with the lower esophagus communicating with the trachea or in rare cases with the bronchus (7) tracheo-esophageal and tracheo-bronchial fistula, without any other anomaly of the esophagus, (8) congenital stenosis a single or multiple stenotic areas b strictures caused by folds or membranes, c pressure from without (9) congenital dilatation due to spasm achalasia or paralysis (10) diverticula (11) cysts (12) congenital shortening with thoracic stomach (13) aberrant tissue

Congenital absence of the esophagus Agenesis of the esophagus is an extremely rare condition Only a few cases have been reported occurring in the human subject Absence of the entire esophagus occurs only in monsters Partial absence of a segment of the esophagus is occasionally seen The esophagus represented by a solid cord is very rare

Double esophagus Doubling of the esophagus is exceedingly rare It occurs as a complete or partial doubling Partial doubling with bifurcation and reunion at the lower end has been recognized A rare case of a double esophagus and double stomach was reported by Gjorup

Esophageal duplication Congenital esophageal duplications have been described by Ladd and others are cystic structures arising in the posterior mediastinum They are usually intimately attached to the esophagus but in a few reported cases there was no attachment These duplications are lined with esophageal or gastric mucosa Ordinarily there is no communication between the esophagus and the cystic structure

They are usually observed in infancy and childhood The symptoms are those of compression on the adjacent organs Dysphagia cough dyspnea and cyanosis are the predominant symptoms encountered The roentgen examination yields evidence of a mediastinal mass simulating a tumor It displaces the esophagus mediastinum and heart The cystic structure is smooth in contour and usually spherical Occasionally it may erode the vertebra or adjacent ribs Barium administered on fluoroscopic examination reveal the mass adherent to the esophageal wall

occurs whereby the receptors of the Hering Breuer reflex are stimulated and inspiration is inhibited constantly Expiration begins before inspiration is completed This may result not only in more rapid and shallow respirations but also in the subjective sensation of air hunger since the urge to breathe is continuous The sensitivity of the vagal nerve endings is thereby not increased (Bruce et al)

Possibly partial compression of some alveolar ducts and alveoli by engorged pulmonary vessels modifies respiration because the reduction of alveolar distension activates the inspiratory neurons

Although some observers hold these reflexes from the pulmonary vessels and the alveolar ducts solely responsible for the appearance of dyspnea in pulmonary congestion other mechanisms undoubtedly contribute

5 In pulmonary congestion the superficial pleural and deep intrapulmonic lymph spaces dilate enormously (Zdansky) Increased venous pressure and lessened respiratory movements of the lungs are responsible for a slow intrapulmonary circulation of blood and lymph Alveolar transudation increases when pulmonary congestion develops rather rapidly and contributes mechanically to the causation of dyspnea The parenteral administration of a mercurial diuretic and the consequent diuresis increase the vital capacity and may afford great relief

6 Chronic pulmonary congestion causes overdistention of the lung (volumen pulmonum auctum) as well as structural changes The amount of connective tissue increases (pulmonary fibrosis) and the alveolar wall may undergo alterations In chronic congestion the capillaries around the alveoli are abnormally wide elongated and tortuous The distended capillaries may permit the passage of five to twenty times as many red blood cells as under normal conditions The capillary basement membrane thickens Hyperplastic connective tissue in the alveolar wall and pericapillary edema displace the capillaries from the alveolar space The thickness of the alveolar wall may increase from 1—3 microns to 30—50 microns (Parker and Weiss) These changes partly explain the increased rigidity of the lung and constitute the anatomic basis for the impaired exchange of gases especially of oxygen In pulmonary congestion of long duration sclerosis is invariably present in the arterioles of the lesser circuit All these changes hamper gas exchange and thereby disturb the respiratory function of the lung

7 Formerly diminished oxygen tension or increased carbon dioxide tension of the arterial blood were assigned important parts in the genesis of pulmonary congestion This theory was relinquished when a number of independent investigators repeatedly failed to find any evidence of arterial hypoxemia in patients with congestion unless pulmonary complications supervened or the condition was terminal The oxygen saturation of the arterial blood is normal (95 – 99 per cent) The carbon dioxide tension of the arterial blood is sometimes slightly reduced (hypocapnia) and even pronounced reductions with signs of tetany are not rare Furthermore recent investigations indicate that the respiratory centers are much less sensitive to lack of oxygen than was formerly believed It is remarkable that dyspnea is often missing in patients with congenital heart disease in spite of the presence of marked hypoxemia

A normal oxygen content in the arterial blood of these patients however does not preclude the possibility that cells in the respiratory centers or in the carotid bodies receive less oxygen per minute than normal slow circulation and diminished output per minute are regular findings in patients with cardiac weakness A lower oxygen content of the jugular venous blood has been found in dyspneic cardiac patients by Raab and McMichael In terminal stages tachypnea shallow breathing and the anatomic changes of the alveolar wall cause lowering of the oxygen saturation of the arterial blood Lactic acid in blood and tissues is increased at rest more so on exertion and strongly stimulates respiration

8 In congestive heart failure the basal metabolic rate increases without any evidence of hyperthyroidism Readings of 40 and 50 per cent above normal are common In cyanotic anoxemic patients the high basal metabolic rate is apparent rather than real because large quantities of oxygen are consumed in order to diminish oxygen unsaturation However the oxygen requirement of the tissues is raised a factor which may occasionally contribute to the development of dyspnea

Increase of the basal metabolic rate occurs in cardiac patients without dyspnea or tachycardia For unknown reasons patients with aortic stenosis may have a basal metabolic rate of 70 per cent above normal in the absence of marked congestion

9 Pulmonary congestion increases intrapleural pressure and lessens the excursion of the diaphragm with respiratory efficiency thus decreased The diaphragm is higher because of meteorism enlargement of the liver or ascites Increased intrathoracic pressure impedes the return of venous blood from the central nervous system to the right atrium and thus is supposed to increase congestion in the respiratory centers

10 Raab considers adrenosympathogenic discharges (epinephrine and norepinephrine) which accompany physical exertion as important in the mechanism of exertional dyspnea

CONCLUDING REMARKS Among these factors the reflexes from the pulmonary blood vessels and alveolar ducts may be considered most important for the appearance of dyspnea in pulmonary congestion Investigations suggest that the dyspnea which occurs physiologically during muscular exertion is derived chiefly from reflexes originating in the skeletal muscles (Comroe Harrison et al) Therefore the old contention that respiration may be influenced by reflexes from all parts of the body rather than from the lungs alone seems to approximate the truth (Vierordt)

If mechanical factors were exclusively responsible for dyspnea morphine which depresses respiration ought to be harmful Clinical experience however shows that the dyspnea resulting from pulmonary engorgement is greatly relieved by morphine probably because the drug reduces the excitability of the centers Accordingly some nervous mechanism reflex or central must play a prominent part The experience that the inhalation of oxygen with the aid of a mask or in an

oxygen tent immediately relieves dyspnea shows that reflexes are not solely responsible and that a diminished supply of oxygen to the tissues plays an impor tant part

Unlike the situation in some pulmonary diseases a cardiac patient does not need an increase of respiration in order to maintain an adequate supply of oxygen to the tissues The abnormal breathing does not serve any useful purpose rather it is purely a manifestation of a dysfunction of the regulatory processes controlling respiration

The physical strain imposed on a patient and the injurious effects of the loss of carbon dioxide (hypocapnia) are harmful consequences of dyspnea Accel erated and deep respiratory excursions enhance the return of blood to the heart augmenting pulmonary congestion thus a vicious circle develops

Orthopnea In the presence of pulmonary congestion dyspnea first occurs only with physical exertion which greatly increases the oxygen requirements of the body As pulmonary stasis progresses the effort necessary to induce dyspnea becomes less and less until the least activity suffices and ultimately the con gestion causes dyspnea even as the patient is at rest At this time he must sit upright and utilize accessory muscles of respiration On lying down intolerable dyspnea and marked cyanosis appear This condition is called orthopnea

For a long time the mechanism of orthopnea was explained as follows In order for the dyspneic patient to bring auxiliary respiratory muscles into action to the best advantage the sitting position is adopted and the shoulder girdle is fixed by grasping the edge of the chair or bed Furthermore in this position the diaphragm descends to a lower level and vital capacity increases

At present other factors are regarded as contributory and perhaps of major importance In the sitting position relatively large amounts of blood (up to 15 per cent) are retained by gravity in the splanchnic system and in the sub cutaneous venous depots of the lower extremities This reduces the return of blood to the lung A reduction of venous backflow diminishes pulmonary con gestion and lessens encroachment on the air spaces If the lung becomes less rigid breathing may proceed with less effort The lungs unfold better The diminished pulmonary distention changes the Hering Breuer reflex as described previously When a patient sits the intrapleural pressure is less negative and this may also reduce the venous return to the chest

Some investigators deny the influence of a change of pulmonary congestion and stress the importance of changes in cerebral blood flow In the supine position the flow of blood from the lower part of the body to the thorax increases this elevates the intra-arterial pressure and tends to impede the inflow of blood from the superior vena cava and its tributaries Increased congestion of the latter may augment congestion of cerebral respiratory centers In the upright position venous pressure near the respiratory centers is more nearly normal Sometimes mere elevation of the head of the supine patient by flexion will give a recumbent dyspneic patient remarkable relief (Ernstene and Blumgart)

PAROXYSMAL NOCTURNAL DYSPNEA CARDIAC ASTHMA AND PULMONARY EDEMA

Occurrence In the early stages of heart failure certain patients do not exhibit dyspnea on exertion The dyspnea occurs at night during rest and often awakens the patient from sleep This variety of dyspnea the paroxysmal nocturnal form is very common As a matter of fact many patients with heart failure *suffer from it since it is encountered in connection with hypertension* nephritis aortic valve lesions coronary sclerosis and in the various myocardial lesions

All these patients have one condition in common namely failure of the left ventricle In hypertension strain is imposed upon the left ventricle which fails first the left ventricle is the structure mainly affected in lesions of the aortic valves in coronary artery disease and in practically all diseases of the myocardium

Patients who suffer from mitral stenosis a tricuspid lesion or pulmonary diseases and who develop heart failure do not complain of these forms of paroxysmal nocturnal dyspnea When these patients suffer from respiratory distress at night it is because they have slipped off their pillows and lie too flat When the elevated position is resumed dyspnea disappears and sleep returns Or as in mitral stenosis a special form of pulmonary edema characteristic for this lesion appears but always under specific circumstances

Some patients assert they have nocturnal dyspnea when actually it is not present they are constantly breathless and dyspnea or orthopnea is present irrespective of time or activity Many patients with left ventricular failure suffer from Cheyne Stokes breathing which as will be discussed later often occurs only at night or undergoes striking accentuation at this time Accordingly the interrogation of the patient must be undertaken carefully to elicit the paroxysmal character of the dyspnea in an unequivocal form

Spontaneous Nocturnal Dyspnea Patients with left ventricular failure may present dyspnea which appears paroxysmally causing hunger for air labored breathing and great anxiety so that sleep is interrupted The attacks subside in ten to twenty minutes and as a rule sleep returns On the next day the episode is regarded as a dream or is forgotten This type of labored breathing is called spontaneous dyspnea (Wassermann)

Cardiac Asthma On a subsequent occasion at times the following night but sometimes after weeks or months the patient is awakened by the same sensation and a similar but more severe attack occurs There is profuse sweating and the cold clammy skin may be cyanotic Breathing is very labored and inspiration as well as expiration is difficult When dyspnea is less pronounced cold sweat may be the chief symptom possibly persisting for a time after the dyspnea disappears If he is able to move the patient may open a window to obtain more air more often he is incapable of such exertion and sits on the edge of the bed with the legs hanging down because this position seems to give some relief A sensation of choking may be extremely distressing *The patient may be*

apprehensive and fear that death is imminent The diagnosis is cardiac asthma (Hope) Although the attack may be severe not rarely the history is entirely negative in respect to previous minor attacks the alarming episode may even develop suddenly in a patient hitherto free of symptoms suggestive of cardiac disease

Examination may disclose that the thorax is held in the inspiratory position an acute overdistention of the lungs is present The auxiliary muscles of respiration are active breathing is rapid and shallow or slow and labored The expiratory phase is prolonged The neck veins are not engorged and the liver is rarely enlarged Rhonchi may be audible over the lungs and moist rales and crepitation are heard at the bases The blood pressure is elevated above the customary level for the patient Sometimes it rises by 60—100 mm Hg Osler found a systolic pressure of 340 mm Hg during the attack in one of his patients It is ominous if the blood pressure previously elevated begins to fall The elevation of blood pressure is the result at least in some cases of asphyxia acting on the centers or causing *peripheral vasoconstriction* The rise of the blood pressure with the tachycardia and profuse perspiration may be caused by an increased secretion of adrenalin and other pressor amines The heart rate is rapid and the rhythm is usually regular The heart sounds are distant and of equal intensity this finding in combination with the tachycardia gives the impression of an embryocardia

The attack may last from thirty minutes to many hours Usually it subsides without treatment A second attack may occur later that night or weeks may elapse before there is a recurrence

While such attacks are predominantly nocturnal diurnal episodes of the same type are not infrequent

The attacks occur without apparent reason Sometimes a heavy meal associated with the consumption of alcohol or large amounts of fluid a frightening dream or reflexes such as those released by a full bladder are considered precipitating factors

It must be questioned whether cardiac asthma actually is an entity In many cases spontaneous nocturnal dyspnea with reflex bronchospasm exists

Pulmonary Edema Many times moist rales suddenly become audible over the entire lung and a brief effortless cough is followed by the expectoration of serous frothy sometimes pink sputum Pulmonary edema has developed Many patients have no asthma some no sputum The dominant features are rather shortness of breath sweating anxiety and a frequent short cough which is ominous and characteristic With the paroxysms of coughing there will also be bubbling in the chest and crepitant and coarse tracheal rales

Occasionally pulmonary edema occurs during the day and it is not an uncommon event during the visit to the physician s office

The onset may be abrupt and the danger of asphyxiation is grave owing to the profuse secretion of serous fluid in the air passages at times it literally gushes from the nose and mouth In other cases paroxysms of coughing may last for hours without copious exudation

Patients with left ventricular failure who develop attacks of pulmonary edema every night may be free from attacks for four to five nights in succession if a profuse diuresis is brought about by the use of a diuretic

An attack of mild pulmonary edema may suddenly change into a severe attack or be followed by shock The breathing may become gasping and gradually *appears more and more superficial*

Irrespective of the clinical manifestations the attack may subside without medical intervention and as in cardiac asthma leave the patient profoundly exhausted Usually the temperature is elevated at times it may rise to 39 C in the first twenty four hours

Pulmonary edema is discussed in greater detail on p 15 Its therapy is discussed in the final chapter of the book

Interrelation between these Attacks These three kinds of dyspnea — namely mild transient nocturnal spontaneous dyspnea cardiac asthma and pulmonary edema — merge into each other without sharp differentiation Consequently some of these terms such as pulmonary edema and cardiac asthma have been used interchangeably Moreover the different types may appear in the same patient on successive nights and apparently they are evoked by similar mechanisms For these reasons the three varieties of paroxysmal nocturnal dyspnea will be considered together in the following remarks and keeping their mutual characteristics in mind cardiac asthma will receive greater emphasis

Pathogenesis of Cardiac Asthma

Mechanical Theory Even the first investigators interested in the mechanism of cardiac asthma were impressed by the fact that damage or at least enlargement of the left ventricle was a regular phenomenon in these patients According to the classical explanation occasionally the right ventricle functions properly while the left is unable to transfer all the blood from the lesser circuit into the systemic circulation The pulmonary vessels become engorged and overdistended so that pulmonary rigidity and dyspnea develop Actually in the intervals between attacks patients suffering from paroxysmal nocturnal dyspnea usually show clinical or roentgenologic evidence of pulmonary congestion

Strong reasons were soon advanced against the conception that simple mechanical engorgement of the pulmonary vessels causes the paroxysmal attack of dyspnea For example it is difficult to explain by this hypothesis why the attacks usually appear at night or during complete rest that is when the working conditions for the left ventricle are better than those existing during the day A postman may walk many miles during his daily rounds without dyspnea during rest at night he may be awakened by an attack of cardiac asthma without the least warning On the following day he resumes his customary delivery without discomfort and a week later the attack recurs at night Moreover the attacks may be exclusively nocturnal in patients whose condition compels them to remain at complete rest in bed day and night

Most impressive in this last connection was an army officer who suffered from cardiac decompensation resulting from syphilitic aortic regurgitation A severe ankylosing arthritis which involved most of his joints had developed after a plunge into icy water during military maneuvers and gradually led to complete immobilization Although this patient was immobilized both day and night and was unable to flex or extend an extremity his nights were made horrible by the most severe attacks of cardiac asthma and Cheyne Stokes respiration

If pulmonary congestion alone were responsible cardiac asthma ought to develop most frequently in patients with mitral stenosis because extreme pulmonary congestion is common in this lesion On the contrary it is well known that attacks of cardiac asthma are absent in mitral stenosis while pulmonary edema does occur in these patients it is not the spontaneous paroxysmal nocturnal type (see below section on Pulmonary Edema)

Morphine abolishes an attack of cardiac asthma and pulmonary edema almost miraculously This fact can also be advanced against the exclusive importance of mechanical pulmonary congestion as the cause of the attacks There is no known direct action of morphine on the left ventricle or on the circulation thereby removing pulmonary stasis which can explain the prompt relief the drug affords in an attack

The observations just cited were incompatible with the old conception and could not be dismissed Accordingly the explanation was modified although even recently some observers have attributed the attacks to the mechanical effects of pulmonary congestion alone

Several observations lend support to the theory that paroxysmal attacks of dyspnea are released by an abnormal situation in the respiratory centers and in the reflex respiratory regulation These are (1) the excellent effect of morphine in a paroxysm and the prevention of recurrences by small doses of this drug given prophylactically (2) the appearance of pulmonary edema in various cerebral disorders (3) the lack of parallelism between the occurrence frequency and severity of the attacks with the amount of pulmonary engorgement and within limits the independence of the attack from other signs of congestion (4) the development of cardiac asthma in the same disorders in which Cheyne Stokes breathing is observed and for which abnormalities within the respiratory centers are an accepted fact (5) the sudden onset of the attack and the obvious purposelessness of the deep respirations which differ so markedly from those encountered in pulmonary congestion (6) the accompanying phenomena such as profuse sweating pallor and anxiety (7) the rarity of these attacks in daytime

Chemical Theories It is the task of the left ventricle to supply the tissues with an adequate amount of blood thus guaranteeing sufficient quantities of oxygen and nutrient materials and permitting the removal of carbon dioxide and other metabolites Under otherwise normal conditions and without the intervention of complicated and at times ineffective regulatory devices the immediate result of diminished function of the left ventricle is its expulsion of less blood per

unit of time Consequently, tissue nutrition suffers and cardiac failure leads to local metabolic disturbances An immediate result of diminished oxygen supply is the accumulation of abnormal metabolic products (of nonvolatile acids in general and specifically of lactic acid) Several investigators using different methods have actually demonstrated a diminished stroke volume with a reduction of minute volume and prolongation of circulation time in patients with left ventricular failure The reduction of cerebral blood flow is proportional to the reduction of cardiac output (Scheinberg) Impairment of the cerebral blood supply causes an increased content of lactic acid in the venous blood

Since the respiratory centers and the chemoreceptors in the carotid and aortic bodies respond strongly to these chemical changes respiratory disturbances might originate from these structures It is established that the respiratory centers are sensitive to the stimulus of carbon dioxide while the chemoreceptors respond readily to hypoxemia

Examination of the arterial blood of a cardiac patient however does not disclose less oxygen saturation or larger amounts of carbon dioxide than are encountered under normal conditions On the contrary oxygen saturation is normal unless pulmonary complications are present or the condition is terminal moreover as pointed out before, dyspnea may cause hypocapnia Nevertheless the composition of blood in the vessels may not reflect the true situation in the tissues Hypoxia of the chemical receptors might result from a reduced supply of blood even if its composition were normal The prompt relief of dyspnea following the inhalation of oxygen and the marked oxygen unsaturation of venous blood in such patients shows that tissue hypoxia might have some importance Even when the oxygen saturation of arterial blood is normal inhalation of pure oxygen brings about relief since this augments the amount of oxygen in physical solution This small change might lead to marked improvement Data on oxygen tension and the quantity of accumulated metabolic products (e g lactic acid) in the tissues in normal and abnormal situations are incomplete

It is certain therefore that the examination of the arterial or even the venous blood does not afford reliable conclusions concerning the status of the tissues for example the hydrogen ion concentration in the tissues differs vastly from that of the blood in a variety of experimental conditions The quantity of blood flow rather than the quality of blood may produce the tissue alterations For these reasons it has been asserted that the chemical normality of the blood in the carotid artery or jugular vein in patients suffering from cardiac asthma is not a valid objection to the chemical explanation just cited While the hypoxia in cardiac failure is slight it is important because the centers are very sensitive to the slightest changes

Recently more powerful arguments have been advanced against this chemical theory Increased formation of acid from oxygen deprivation has not been satisfactorily demonstrated (Nielsen) Likewise the centers are much less sensitive to changes of hydrogen ion concentration than hitherto assumed (Schmidt) Proof is also lacking to show that diminished blood supply to the tissues causes

dyspnea for dyspnea is not outstanding in shock or in patients with pericardial adhesions and marked diminution of the cardiac output No cardiac asthma appears in advanced mitral lesions with a small cardiac output The disturbance of respiration induced by acidosis (Kussmaul breathing) differs from the dyspnea of cardiac patients Moreover some patients with cardiac asthma have a normal cardiac output Abnormal acids are conceded to act on the centers only in terminal stages for true hypoxemia and carbon dioxide excess do exist at this time In right heart failure (tricuspid insufficiency mitral stenosis) there is marked peripheral venous stasis with reduction of oxygen tension an increase of carbon dioxide tension and increased lactic acid content of the blood but no dyspnea of the paroxysmal nocturnal type

The Reflex Theory Most recent observers believe that attacks of cardiac asthma and pulmonary edema derive mainly if not wholly from reflexes originating in the lung and released by the pulmonary congestion This causes dyspnea in the manner discussed earlier Reflexes from these receptors may alter the excitability of the respiratory centers and make them more sensitive to carbon dioxide the physiologic stimulus of respiration

Reasons for the Nocturnal Appearance of Attacks

It has always been and still is difficult to explain the predominantly nocturnal appearance of paroxysmal cardiac asthma and pulmonary edema At present no satisfactory integration of the known facts seems possible It is hard to understand why physical effort in many cardiac patients with left ventricular failure with the consequent augmented strain on the left ventricle with the formation of non volatile acids in the blood and with increased pulmonary congestion as well does not elicit the attacks A few factors which may influence the nocturnal appearance of the attacks merit mention

1 Even under normal conditions the tonus of the parasympathetic nervous system increases decidedly during sleep and the influence of vagal tonus and of vagal reflexes on the occurrence of dyspnea is well established The fact that attacks of ordinary bronchial asthma develop more commonly at night is explained on this basis Similarly the greater incidence of gallbladder and renal colic of spasms and tenesmus at night and also the frequent onset of labor pains at this time have been explained by this increase in vagal tone

2 During sleep the carbon dioxide tension in blood and tissues mounts even in healthy people although only to a slight degree This fact is explained by the change in irritability of the respiratory centers which occurs in the absence of peripheral and cortical stimuli The special significance of carbon dioxide as a stimulus of the respiratory centers is universally accepted This physiologic nocturnal accumulation of carbon dioxide is superimposed upon the pathologic conditions prevailing in the centers although either factor alone constitutes only a weak stimulus in combination they may suffice to provoke an attack of dyspnea

3 During the day higher cortical areas continuously influence the respiratory centers promoting depressing or modifying their activity Respiration can be altered voluntarily and mental excitement as well as things seen heard or felt influence its rate and depth All these predominantly stimulating influences are absent at night When respiratory centers are left to themselves they may permit the development of local changes which would be instantly corrected during the day by increased respiration The diminished irritability of the centers during sleep permits the lungs to become more congested

4 Normally such circulatory values as the pulse rate and blood pressure fall at night and accentuate any slowing of circulation already present (Kroetz)

5 Tissue fluids pass into the blood at night (Brunn) a factor which is considered responsible for the nocturia of patients with heart failure The plasma volume increases because of the absorption of latent edema Recurrent attacks of pulmonary edema vanish without any other therapy if the patient receives a mercurial diuretic on the contrary pulmonary edema recurs when fluid is retained and reaches a certain level Furthermore the importance of water retention is emphasized by the frequent precipitation of attacks of pulmonary edema by the ingestion of large amounts of fluid

6 Rest in bed promotes the return of blood from the lower part of the body and other things being equal tends to accentuate pulmonary congestion in patients with left ventricular failure Sudden movements in bed or the transient hyperpnea during an exciting dream can increase the influx of blood from stagnant areas and thus augment pulmonary congestion

The disappearance of attacks without medical intervention is much more difficult to explain If the attack is attributed to the effect of abnormal stimuli on the centers or chemoreceptors blowing off of carbon dioxide and inhalation of larger amounts of oxygen would serve as an explanation The end of the attack is incomprehensible if it is provoked exclusively by pulmonary congestion and reflexes Overactivity of the sympathetic nerves or an increased output of pressor amines which cause the pallor and sweating of the patient and which is at least in part the reason for the hypertension during the attack may be responsible

The beneficial effect of morphine is readily explained on the basis of all theories which concede primary importance to the condition of the nerve centers or reflexes

Differential Diagnosis between Cardiac and Bronchial Asthma

The differentiation of cardiac from bronchial asthma is a difficult problem and one of great practical importance Not only is the prognosis of these two conditions vastly different but treatment is based on the distinction While epinephrine is usually valuable in an attack of bronchial asthma it is contraindicated in cardiac asthma On the other hand the specific therapeutic agent for cardiac asthma morphine is dangerous in bronchial asthma Accordingly a distinction between the two disorders is of paramount importance in an acute

attack although making such a distinction sometimes meets with unsurmountable obstacles

A carefully obtained history often but not invariably helps in the differentiation It may be devoid of value or unobtainable if the patient is seen during his first attack

Reference was made earlier to the fact that cardiac asthma may strike unexpectedly and without previous warning If careful interrogation reveals that the patient has no complaints referable to the heart or if an examination during the attack fails to disclose any distinct evidence of cardiac damage the differential diagnosis may be impossible during the seizure

Satisfactory examination of the heart during either kind of attack may be difficult Accurate percussion is impossible owing to the acute dilatation of the lung or chronic emphysema The emphysema the rales and the inability of the patient to hold his breath render auscultation difficult In both conditions the electrocardiogram may show only slight changes and usually it is not immediately available Often expiratory dyspnea is equally pronounced in both types of asthma As a rule the blood pressure is elevated during an attack of cardiac asthma whereas with bronchial asthma the blood pressure is generally low however hypoxemia may cause the blood pressure to rise in an attack of bronchial asthma so that it is improper to establish the diagnosis on this sign alone While it is a good rule to suspect cardiac asthma if the first attack develops in a patient of more than sixty years bronchial asthma may also develop at this age cardiac asthma may occur of course in much younger individuals Not rarely particularly in elderly individuals pulmonary and circulatory causes for dyspnea coexist and both forms of asthma may appear In such cases it becomes difficult to evaluate the mechanism of an attack

Examination after an attack subsides usually provides more information to establish the diagnosis Nevertheless it must not be forgotten that many lesions associated with cardiac asthma do not produce murmurs or cardiac enlargement and that patients may have an eosinophilia in the peripheral blood following an attack of cardiac asthma Therefore mistakes in both directions are common Sometimes prolonged observation is necessary before a decision is possible In these cases the determination of the circulation time may be helpful since it is normal in bronchial asthma and prolonged in most cases of cardiac asthma

Bronchospasm with asthmatic attacks occurs in patients with acute or chronic pulmonary congestion and such seizures are explained by a reflex spasm released from the congested vessels This thesis is supported by the immediate improvement following an intravenous injection of aminophylline in these patients Bronchial asthma may be a serious complication in the course of cardiac decompensation particularly in patients having coronary thrombosis with infarction and pulmonary congestion In a series of 250 cases of cardiac asthma an allergic asthma coexisted in five (Palmer and White) Treatment without epinephrine was difficult and all succumbed Sometimes epinephrine must be given to patients suffering from both cardiac and bronchial asthma despite

the associated cardiac hazard. This is permissible however only when the administration of aminophylline in large doses has failed to relieve the attack. In general aminophylline is the remedy of choice for all patients with asthma when the differential diagnosis is not immediately possible.

Pulmonary Edema

The clinical picture of pulmonary edema in left ventricular failure and its close relation to cardiac asthma has been described above.

Pulmonary edema is not an entity. Apart from the type resulting from left ventricular failure there are other varieties which deserve brief consideration.

The Types of Pulmonary Edema (1) Pulmonary edema is observed in lesions of the nervous system as exemplified by skull fractures injuries of the cervical spine encephalitis brain tumors intracranial (subarachnoid) hemorrhage embolism and meningitis. The permeability of the pulmonary capillaries has been said to be subject to central regulation. In pulmonary edema of neurogenic origin produced experimentally changes of the blood pressure and other disturbances of cardiodynamics may be responsible. It is of interest that veratrine given intravenously in minimal amounts to rabbits causes no effect. When the same substance is injected suboccipitally pulmonary edema appears within a few minutes (Jarisch et al.)

2 In coronary thrombosis pulmonary edema may develop suddenly irrespective of antecedent anginal pain. Its appearance has been attributed to reflexes (Fuisada).

In patients with myocardial infarctions we observed attacks of pulmonary edema occurring on the slightest provocation such as excitement or exertion but more often spontaneously at night without any apparent reason. These attacks may occur over a period of many months even after patients resumed their work. They appear without changes in the electrocardiogram or any sign on physical examination indicating new infarctions. They appear sometimes nightly at the same hour. They are observed without roentgenologic evidence of pulmonary congestion and cardiac enlargement. They disappear suddenly.

3 Pulmonary edema may develop at the beginning of a pneumonia or other inflammatory process in the lungs such as bronchitis particularly in elderly subjects and in those with pulmonary congestion. The release of histamine from the affected tissue and the altered permeability of the vascular endothelium and alveolar wall explain this form.

4 Pulmonary edema resulting from the gases used in chemical warfare is well known. Thus one or two deep breaths of a concentrated sample of phosgene may produce a lethal pulmonary edema. The symptoms appear after a latent period which may last nine hours. Here too changes in permeability of the vascular endothelium and the release of histamine in the tissues are considered responsible for the appearance of this kind of pulmonary edema. The ... on of acids in the tissues hydrochloric acid from phosgene or nitric ac... fumes may play a role

5 A very interesting form of pulmonary edema though fortunately rare may be encountered in certain cases of mitral stenosis in the absence of atrial fibrillation marked enlargement of the left atrium evidence of right heart failure or passive congestion in the liver If the congestion increases as the result of excitement or exertion and the intracapillary hydrostatic pressure exceeds the oncotic pressure of the plasma proteins pulmonary edema develops

It is easy to distinguish this form from the ordinary form of pulmonary edema of left ventricular failure These patients (usually women) develop one or more attacks daily during ward rounds while in the hospital or in the course of an animated conversation or walking a short distance on level ground or during sexual intercourse Presumably the propulsion of large volumes of blood into the lesser circuit which accompanies the acceleration of the heart rate in such cases increases pulmonary engorgement (pulmonary capillary pressure) sufficiently for edema to appear If the right ventricle functions well and the stenosis of the mitral valve is advanced the pulmonary congestion is extreme These patients must always have morphine available and sometimes it must be administered *prophylactically so that an examination may proceed without an attack* With longer duration of pulmonary congestion in mitral stenosis the attacks of pulmonary edema disappear Increasing sclerosis of the pulmonary vessels and fibrosis of the lungs make transudation of plasma impossible even if pulmonary congestion increases Thus this form of pulmonary edema is seen only under certain conditions in patients with mitral stenosis which is not too advanced It will be discussed in Chapter 12 in the section on this valvular lesion

The form of pulmonary edema which appears postpartum in patients with mitral stenosis is exceedingly dramatic Often the valvular lesion is so mild that the patient and family are unaware of its existence Since fatalities are not uncommon and are often unanticipated this catastrophe will never be forgotten *by anyone who has witnessed it The sudden return of* large amounts of blood from the pelvic veins to the heart and lungs seems to be responsible for the attack In this type of pulmonary edema the importance of increased intracapillary pressure as an initiating factor is evident

6 Pulmonary edema with hemorrhagic sputum may be noted during attacks of paroxysmal tachycardia We have seen them recur with every paroxysm in otherwise healthy persons This form cannot be easily explained by pulmonary congestion since the tachycardia affects the right and left ventricle equally and pulmonary congestion does not develop in these cases The patient exhibits only venous congestion and enlargement of the liver (inflow stasis) owing to the shortening of diastole Some experimental results show however that an abnormal spread of the excitation wave *during paroxysmal tachycardia* may alter contractility of one ventricle more than that of the other (Wiggers)

7 Following the administration of large quantities of fluid (saline glucose solutions) as recommended after operation in certain cases pulmonary edema is not rare Vagotomy with forcing of fluids is a well known experimental method for eliciting pulmonary edema in animals We have seen this variety (sometimes

combined with cerebral edema) following large transfusions postoperatively particularly in patients with hyperthyroidism Fortunately warnings have been sounded against the abuse of forcing fluids intravenously particularly in patients with cardiovascular disorders

8 Sometimes pulmonary edema may appear following thoracocentesis and the removal of large amounts of fluid This form has been called edema ex vacuo When the pressure on the pulmonary vessels is suddenly released a reactive hyperemia with copious transudation may cause inundation of the lung

9 In pheochromocytoma an acute pulmonary edema during a hypertensive crisis may be the first sign of the disease Sometimes it is lethal

10 Pulmonary edema may appear as a manifestation of pulmonary embolism

11 Often overlooked is the acute or chronic pulmonary edema in acute nephritis The edema seen in azotemia is usually and perhaps invariably caused by heart failure Many patients with pure azotemia do not exhibit pulmonary edema

12 Pulmonary edema appears occasionally after the injection of the contrast medium for angiocardiography

13 Finally terminal pulmonary edema must be mentioned It occurs in the last minutes or hours of life in connection with a host of diseases

Acute and Chronic Forms of Pulmonary Edema In many cases of acute pulmonary edema the onset of symptoms is abrupt Fluid fills the lungs in a few minutes and the patient practically drowns from the copious collection of serous fluid in the air passages Sometimes subacute pulmonary edema exists It is heralded by cough which gradually increases in intensity and profuse sweating Early examination of the lungs reveals ominous crackling rales In chronic pulmonary edema severe dyspnea moist rales and rose colored sputum may exist for many days

Roentgenologic examination is invaluable in the diagnosis of the chronic or subacute types of pulmonary edema The lung fields diffusely darken and cloudlike shadows appear While the roentgenologic signs are more accentuated at the site of a pleural adhesion in pulmonary congestion (this holds for the clinical signs as well) the lung fields near an adhesion are much clearer in the case of pulmonary edema (Zdansky) If the pulmonary edema is localized often no evidence of congestion is found in the nonedematous areas This indicates that congestion is not necessarily a precursor of pulmonary edema In the chronic forms the edema may be limited to the central (circumhilar) area and therefore escapes discovery on physical examination (figure 1) Often it is more pronounced in the interstitial spaces rather than free in the alveoli and therefore also tends to elude detection by auscultation In this form there are no symptoms Pleural effusions are common in the chronic type

Pulmonary edema may be found in only *one* lobe The apices the bases near the diaphragm and also a small peripheral area near the chest wall often are free from opacities Small shadows or dense circumscribed cloudlike shadows cannot easily be differentiated from primary or metastatic carcinoma or from pneumonia

(figure 2) In uremia a similar distribution of edema occurs when cardiac failure supervenes Also typical is the interstitial edema with the butterfly pattern spreading in all directions from the hilus

Figure 1 shows the typical edema of a patient with hypertension without azotemia The left ventricle is enlarged a butterfly pattern exists while the



FIG 1 Chronic pulmonary edema with typical hilar butterfly pattern The patient suffered from hypertension without azotemia

peripheral parts of the lungs particularly the apices and bases are clear Figure 2 shows dense shadows imitating pulmonary metastases

Mechanism A slow transudation of fluid takes place normally in the lungs This fluid is however evaporated during aeration In pulmonary edema increased permeability of the vascular endothelium must be assumed (Drinker) as the *protein content* of the edema fluid is great (2—4 per cent)

The importance of an increase of the fluid content of the lungs in the appearance of pulmonary edema has been stressed earlier. Equally important is the permeability of the vessels and perhaps also of the alveolar wall. If pulmonary congestion is rather acute, the lungs are moist and much fluid exudes when they are sectioned at necropsy. The brown indurated lungs present in the chronic congestion of mitral stenosis are, however, dry. This is readily explained by the



Fig. [illegible] Pulmonary edema with dense shadows in the right and left lung in a 22 year old patient with chronic nephritis without *azotemia*

progressive pulmonary fibrosis associated with the secondary sclerosis of the vessels of the lesser circuit; this makes transudation of fluid impossible despite marked congestion. It also explains why pulmonary edema and hemoptysis occur in early but not in late stages of mitral stenosis. Anoxia widens the capillaries locally and increases their permeability.

Consequences. Profuse pulmonary edema may secondarily influence the circulation and the condition of the patient in other ways. Transudation of large volumes of serum into the lungs may cause dehydration since the amount of fluid lost in this way may be enormous. In the pulmonary edema of phosgene poisoning the weight of one lung may exceed 1 250 grams, that is, more than five times the normal weight. It has been estimated that as much as one half the plasma volume ma

be lost in extreme cases this causes the red blood cell count and hemoglobin to rise the blood nonprotein nitrogen to increase and a general acidosis to develop in the same way as after a severe burn of the body surface The mechanical obstruction of the air passages by edema fluid may cause asphyxia

In some attacks the blood pressure falls the pulse becomes thready respiration gasping and shock appears during which the patient expires

If the reflex tachypnea in a patient with pulmonary edema (and even in cardiac asthma) assumes a rapid and shallow character the tidal air may be reduced to 250 cc or even less Since about 150 cc are needed to fill the dead space gas exchange in the lung suffers Hypoxia may ensue in a few minutes resulting in even more rapid and shallow breathing During such tachypnea the oxygen unsaturation of the blood may amount to 40–50 per cent Accordingly changed arterial oxygen saturation may be the result rather than the cause of dyspnea

Hyperventilation may reduce carbon dioxide tension of the blood (hypocapnia) causing a shocklike syndrome with symptoms of tetany This dyspnea fails to serve any useful purpose and imposes a heavy burden on a heart already strained Moreover it increases the oxygen consumption of the body which is greater from the start owing to the high metabolic rate of cardiac patients

Functional Disturbances of Other Vegetative Centers in Paroxysmal Dyspnea

As with patients with Cheyne Stokes respiration those persons who suffer from cardiac asthma or pulmonary edema may exhibit a series of other respiratory phenomena These disturbances are also prone to occur at night and may be coincident with or independent of the paroxysmal episodes

An early sign of left ventricular failure is nocturnal cough While it represents a typical complaint in pulmonary congestion sometimes it develops in patients with progressive left heart failure before pulmonary congestion can be detected clinically It causes considerable discomfort and is often treated for a long time with cough medicines before its true nature is recognized The administration of digitalis usually abolishes it in a short while

Persistent sighing and yawning are frequently noted in patients with left ventricular failure Patients rarely complain about these symptoms but they are readily discovered Like the cough these phenomena vanish after a short course of digitalis therapy Since the yawning and sighing observed after an acute profuse hemorrhage are generally attributed to cerebral anemia that is to a diminished blood supply to the cerebral centers it is conceivable that a lessened cardiac output and slow peripheral circulation have a similar effect

The various respiratory phenomena just mentioned make patients with left ventricular failure extremely restless and noisy During ward rounds the physician often becomes aware of such a patient even when he is some distance away

Naturally left ventricular failure would never be diagnosed on the basis of these symptoms alone because other factors are more commonly responsible for

their appearance. They are mentioned merely to emphasize that vegetative centers in the neighborhood of the respiratory centers also function abnormally in left ventricular failure.

Concluding Remarks

The available evidence indicates that no single factor is exclusively responsible for attacks of paroxysmal nocturnal dyspnea. The various mechanisms and the interaction of multiple factors may explain why the character of the individual attacks varies. Thus the amount of fluid in the pulmonary parenchyma, the increased intracapillary pressure, the permeability of the pulmonary capillaries and of the alveolar epithelium, subject to central regulation as well as to local changes, may explain the presence or absence of pulmonary edema during an attack of cardiac asthma. Certainly the importance of reflexes on respiration has been grossly underestimated in the past, a mistake partly understandable since some of these reflexes have been discovered only recently. On the other hand an accreditation of the significance of these reflexes should not relegate the local situation in the lungs and the chemical regulation of respiration to a minor position.

Paroxysmal dyspnea may appear early in heart failure when cardiac dilata[illegible] and evidence of congestive failure is absent. Patients with hypertension *of* [illegible] *ing etiology and those with coronary sclerosis may have such an attack* as [illegible] alarm. Just as peripheral edema is no index of the degree of cardiac fa[illegible] frequency and severity of paroxysmal nocturnal dyspnea affords [illegible] conclusion as to the extent of myocardial damage.

It is not clear why failure of the left ventricle alone causes par[illegible] turnal dyspnea; one might anticipate that all types of failure would [illegible] discrepancy presents great difficulties to those who believe that th[illegible] released exclusively by reflexes set in action by pulmonary con[illegible] congestion is certainly very marked in mitral stenosis and yet th[illegible] absent even in button hole mitral stenosis with an almost impr[illegible] and a marked reduction of minute volume. In the recent literat[illegible] stenosis, attacks of paroxysmal dyspnea are said to appear frequ[illegible] lesion, but we shall see in the section devoted to this valvular dis[illegible] not the case. The attacks also fail to appear in right ventricular fa[illegible] ple in severe tricuspid lesions; under these circumstances pulm[illegible] may be negligible although the minute output of the heart is [illegible] peripheral circulation remarkably slow.

Cardiac asthma may disappear when right heart failure sup[illegible] recur if the latter is successfully treated.

Presumably the different factors discussed in the precedin[illegible] pulmonary congestion with its direct mechanical and reflex eff[illegible] chemical status of the centers and of chemoreceptors participa[illegible] of paroxysmal nocturnal dyspnea observed in left ventricular fa[illegible]

CHEYNE STOKES RESPIRATION

Fully developed Cheyne Stokes respiration with continual alternation of apnea and dyspnea is easily discovered when the apnea is prolonged and marked hyperpnea characterizes the dyspneic period Cheyne Stokes respiration is however often overlooked although it is one of the most constant and early signs of left ventricular failure During the examination it may exist in a fragmentary form and may be discernible only if looked for

Clinical Picture

In the consulting room and at home patients often fail to exhibit periodic breathing despite a thorough examination since the least excitement or physical exertion may abolish it If the patient can be induced to relax or to rest with closed eyes in a quiet room for only a few minutes periodic breathing may soon appear Sometimes there is no alternation of breathing and periods of apnea but a mere change from deep to more superficial breathing All gradations from a slight waxing and waning of the respiratory excursions to fully developed Cheyne Stokes can occur

Figure 3 was obtained from a patient fifty eight years of age who suffered from coronary sclerosis The upper tracing shows the periodic change from superficial to deep respiration The lower tracing was obtained a few minutes later when the patient relaxed and became more accustomed to the use of the spirometer dyspnea and apnea alternate In this tracing the lever moves downward with *inspiration*

Figure 4 shows a spirogram obtained from the abdomen (upper tracing) and chest (lower tracing) of a patient with hypertension and left ventricular failure In this tracing inspiratory movements are directed upward Whereas the apneic periods are short in figure 3 the dyspneic and apneic periods are almost equal in figure 4 The former situation seems more common Each phase may last as long as 50 seconds

The characteristic gradual increase of amplitude and the tendency of the chest to assume the inspiratory position in the crescendo phase are visible in both figures *This accounts for the slow rise of the curve in the dyspneic phase (depression in figure 3)* and the gradual reversion to the normal position in the decrescendo phase before the dyspnea begins Apnea usually occurs in the expiratory position In a given case the number of respiratory movements in each phase may remain constant for a long time

In addition to the periodic changes of respiration various other signs may be observed in patients with Cheyne Stokes breathing They likewise come and go periodically and are bound to a certain phase of respiration Thus the pupils may contract at the onset of apnea the blood pressure may increase in the dyspneic phase and arrhythmias such as extrasystoles and paroxysmal ventricular tachycardias may appear periodically Bradycardia may be noted in the apneic phase and tachycardia in the dyspneic phase the opposite situation may also

Fig 3 Cheyne Stokes respiration in a patient with coronary sclerosis

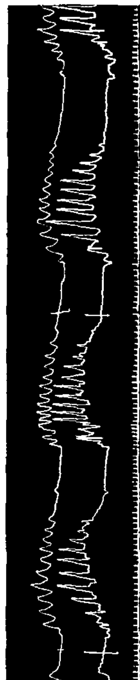


Fig 4 Cheyne Stokes respiration The upper tracing was obtained from the abdomen the lower from the thorax

prevail No fixed rules have been discovered for the appearance of most of these changes in one or the other phase of respiration Somewhat more constant is cough or deep sighing which may develop regularly during the crescendo phase of the dyspneic period

The patient s behavior may change with the different periods In well marked Cheyne Stokes breathing restlessness and involuntary movements of the limbs with twitching and clonic convulsions may be noted during dyspnea whereas the patient is fully relaxed with the eyeballs turned up as in coma during the apneic period Clouding of consciousness is not rare during apnea Delusions of persecution or a syndrome resembling amentia may occur and require commitment to a special institution

Periodic breathing is a normal phenomenon in infants (especially premature ones) during sleep in healthy elderly people and in normal subjects at high altitudes It is also observed in animals during hibernation Patients with sclerosis of the cerebral arteries frequently exhibit it Left ventricular failure is its most common cause Periodic breathing is conspicuously absent in patients with mitral or tricuspid lesions and in those with pulmonary disease and cor pulmonale

The assumption that Cheyne Stokes breathing is an ominous sign is often true however a very pronounced form may occur transiently in patients with coronary sclerosis and myocardial infarction until the left ventricle regains its strength If this happens the patient may remain free from respiratory embarrassment and other symptoms for many years Therefore the prognosis depends upon the underlying etiology rather than on the mere presence of the phenomenon

The absence of Cheyne Stokes breathing during the examination and despite a special search does not preclude episodes of nocturnal periodic breathing with extreme hyperpnea and when it is present during the day it tends to be more severe at night

The periods of hyperpnea may be associated with extreme anxiety and air hunger so that the patient cannot rest He suddenly sits up looks around in despair and utilizes all auxiliary muscles for breathing In a few seconds he relaxes lies down quiet or unconscious in apnea only to have the cycle repeated in a short time This situation may persist for hours and recur night after night When the attacks are milder the patient may leave his bed and restlessly pace the floor

Some patients with Cheyne Stokes breathing do not complain of dyspnea and deny any breathlessness despite the existence of long apneic periods These patients do however suffer from insomnia usually the result of the restlessness which to them is incomprehensible Accordingly many mention only the insomnia the actual cause of which is overlooked If examination fails to disclose Cheyne Stokes respiration careful interrogation of the attendants or relatives and sometimes even of the patient may reveal the presence of rhythmic changes in the depth of respiration

The possible existence of Cheyne Stokes respiration must be considered in every case of nocturnal dyspnea and every effort should be made to establish the diagnosis for this permits the introduction of effective specific treatment which speedily abolishes otherwise intractable complaints The therapy is discussed in the final chapter

Pathogenesis

No explanation for the pathogenesis of periodic breathing is entirely satisfactory All theories assume a changed excitability of the respiratory centers Slow circulation and local vascular disturbances (which provoke Cheyne Stokes breathing in cerebral vascular sclerosis and increased spinal fluid pressure) might produce hypoxia The apnea induced by depression of the centers is assumed to allow the accumulation of carbon dioxide and perhaps of nonvolatile acids which excite dyspnea when a certain threshold is reached During the dyspneic period carbon dioxide is removed from the blood and the hypoxia disappears Since the elimination of carbon dioxide removes the strongest stimulus for the respiratory center apnea returns

This conception leaves much unexplained While the mechanism of the fully developed Cheyne Stokes breathing becomes clear its beginning remains obscure Sometimes the apneic periods are very long while the dyspneic periods are exceedingly short in fact the periods of dyspnea may be so short that they can scarcely permit the elimination of accumulated metabolites Pryor as well as Gilmore and Kopelman are of the opinion that the prolongation of the circulation time in patients with Cheyne Stokes breathing is of primary importance Delayed passage of blood from the lungs to the arterial chemoreceptors and the respiratory centers permits an overventilation irrespective of the cause to last longer Therefore apnea must follow which in turn must be followed by dyspnea

In dogs Cheyne Stokes breathing could be produced by insertion of a delay system between heart and brain (Guyton et al) Normally with physiologic changes of respiration the oxygen and carbon dioxide content of the blood changes this altered blood reaches the respiratory centers quickly and regulation sets in When the circulation time of the blood is delayed the respiratory centers are reached after a longer interval This permits marked changes of the blood gas concentration to develop which as soon as they reach the centers provoke great changes of the respiration

The importance of hypoxia in Cheyne Stokes breathing is shown by the fact that periodic respiration may be induced in normal subjects if they breathe an oxygen poor mixture Moreover the Cheyne Stokes respiration of cardiac patients usually although not invariably disappears when oxygen is inhaled

The experience that Cheyne Stokes respiration may appear only during sleep or be aggravated then speaks in favor of cortical participation in its development This view has some experimental support (Schoen)

During Cheyne Stokes breathing the carbon dioxide tension must be low Hypoxia in combination with high carbon dioxide tension does not cause Cheyne

Stokes breathing Thus Cheyne Stokes respiration in a cardiac patient usually vanishes when a mixture containing 5 per cent carbon dioxide is inhaled and this may be the reason why patients with pulmonary emphysema practically never have this form of periodic breathing even when fully decompensated The reflex dyspnea of patients with mitral stenosis and pulmonary congestion prevents the appearance of Cheyne Stokes respiration

An objective survey of the medical literature discloses that most observers who deny the possibility that hypoxia in the respiratory center might play any part in the mechanism of other types of dyspnea readily concede its primary importance in Cheyne Stokes respiration This is somewhat paradoxic since Cheyne Stokes breathing often antedates other forms of dyspnea and appears in patients subject to recurrent attacks of cardiac asthma Cheyne Stokes breathing occasionally disappears as soon as sleep deepens perhaps because acidosis becomes greater (East)

The role played by a diminished blood supply to the centers in the genesis of Cheyne Stokes breathing is stressed by the following observation Otherwise healthy young individuals with paroxysmal tachycardia and a rapid ventricular rate may present Cheyne Stokes respiration for the duration of the tachycardia When the heart rate reverts to normal Cheyne Stokes respiration vanishes immediately The great reduction of the minute volume in such tachycardias is well known That the excitability of the respiratory centers is a determining factor for the appearance of Cheyne Stokes respiration is indicated by the periodic breathing of many young individuals after the administration of morphine

Periodic breathing resembling Cheyne Stokes respiration also occurs in patients with the Morgagni Stokes Adams syndrome when attacks follow each other at short intervals In this condition dyspnea follows cardiac standstill This is understandable since hypoxia and the accumulation of acid metabolites during the period of cardiac arrest may reach a point where they constitute an unusually strong stimulus for the respiratory centers and chemoreceptors Respiration ceases with the reappearance of the first pulse because hyperventilation during the period of cardiac standstill blows out large quantities of carbon dioxide from the blood in the lungs with the resumption of cardiac action after the standstill this acapnic blood reaches the respiratory centers and the stimulus for respiration is so weak that apnea results If the cardiac standstill recurs every few minutes as sometimes happens hyperpneic and apneic phases alternate so that the respiratory syndrome cannot be distinguished from ordinary Cheyne Stokes Usually the dyspneic phase coincides with cardiac standstill while the heart beats during the period of respiratory arrest

DYSPNEA IN CARDIAC NEUROSIS HYPERVENTILATION SYNDROME

A highly characteristic form of dyspnea is common in patients with nervous instability neurocirculatory asthenia anxiety neurosis and hysteria The breathing is typically irregular and sometimes accelerated so that it might be com

pared to the rapid irregular pulse of atrial fibrillation The continuous change of depth rate and level of respiration readily distinguishes it from other forms of dyspnea from the typical crescendo and diminuendo of Cheyne Stokes breathing from the slow respiration of increased intracranial pressure the transitory arrest of respiration without changes in depth (Biot type) and finally from the Kussmaul breathing of acidosis

Sometimes the respiration of patients with a cardiac neurosis resembles that seen in healthy subjects who on request breathe as fast as possible The same type of breathing may be noted in patients under the influence of some great emotional strain such as the unanticipated death of a close relative Dentists sometimes observe this type of dyspnea preceding an extraction or some other operation

Since rapid and superficial respirations may reduce the tidal air to 250 cc or less the volume of gases available is insufficient for a normal exchange Acute hypoxia thus results

Hyperventilation Syndrome In the hyperventilation syndrome faintness dizziness tingling of the fingers sense of impending death and even loss of con sciousness may appear Patients may experience palpitation dysphagia anxiety tightness about the chest or a dull pain in the lower anterior chest wall Hyper ventilation due to encephalitis or poisoning with salicylates may lead to the same syndrome (Lewis) These patients feel cold and clammy when touched

Peripheral and peri oral paresthesias appear related to respiratory alkalosis The low carbon dioxide content of the arterial blood leads to constriction of smaller vessels causing among other phenomena cerebral hypoxia Signs and symp toms of tetany appear

If the respiratory excursions increase but slightly in rate while their depth becomes greater larger quantities of carbon dioxide are blown off so that hypocapnia and alkalosis develops Want of carbon dioxide may cause the *larger* peripheral vessels including the veins to dilate so that larger amounts of blood are retained in the venous depots Consequently the amount of blood returned to the heart is reduced the pulse becomes small or even impalpable the blood pressure may fall the neck veins fill poorly and a shocklike syndrome may appear We have been repeatedly summoned to see patients who were supposed to have developed shock or circulatory failure following an operation but who exhibited only this syndrome

Individuals who present this type of respiration frequently suffer from sighing respiration as well The latter is discussed below

Holding the breath rebreathing into a paper bag or the inhalation of 5 per cent carbon dioxide help Treatment of a psychoneurosis is often necessary

Electrocardiographic changes during hyperventilation have been repeatedly described They are not due to alkalosis (Scherf and Schlachman)

DYSPNEA IN ENDOCRINE DISORDERS

Patients who have sighing respiration (suspirious respiration) often com plain of dyspnea This does not apply to those who sigh deeply because of grief or

sorrow nor when a sigh is taken to relieve mental tension but it is true in another large group of patients with sighing respiration The patient usually a woman complains that the breath will not go through or that the breath goes only so far (pointing to the upper third of the sternum) or that she is unable to take a deep breath Great relief is secured once she succeeds in breathing deeply (the sigh) Sometimes the complaint of breathlessness is reported with considerable excitement and apprehension Patients are rarely aware that they are compelled to sigh periodically

Figure 5 reproduces a spirogram obtained during the determination of the basal metabolic rate of a 29 year old woman A deep sigh occurs after 3 to 5 normal respirations Apart from the deep sighs there is no irregularity in rate or

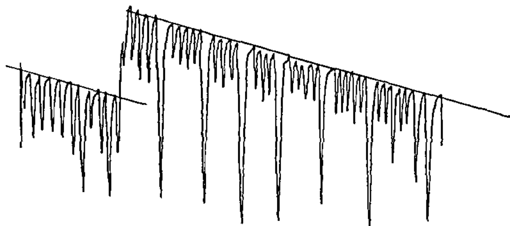


FIG 5 Sighing respiration

depth of respiration Sometimes the sigh may occur after every second or third respiration for a time or alternate with a normal respiratory excursion (respiratio alternans) Since the preceding as well as subsequent respirations are unchanged the deep breath is not compensatory

The deep sigh represents a maximal respiratory effort and corresponds closely to the vital capacity It will frequently be discovered if spirograms or basal metabolism tracings are inspected with this phenomenon in mind It is more pronounced in the recumbent position Christie found such sighs in 6 9 per cent of 1 500 consecutive respiratory tracings In 2000 successive spirograms investigated by one of us sighing respiration was found in 68 only two of these patients were males One of these men had undescended testes Thirty five of the females were beyond 35 years of age and had symptoms suggestive of disturbed ovarian function All but three of the other patients were listed as examples of hyper or hypothyroidism uterine fibroids functional disorders of the nervous system and endocrine imbalance

In the few investigations devoted to it sighing respiration has usually been considered a sign of neurosis and its great incidence in neurocirculatory asthenia

is stressed While patients with neurocirculatory asthenia often display this type of breathing it is a common and regular finding in women with hypo ovarianism It is observed in adolescents and it is particularly prominent at the climacterium even in women over 60 years of age awareness of its occurrence in these conditions will prevent serious diagnostic errors

Sighing respiration certainly does not result simply from estrogen deficiency for it appears in patients suffering from such other disorders as hyper and sometimes hypothyroidism and it is often absent after panhysterectomy It is interesting that the phenomenon is infrequent in males Presumably the endocrine imbalance which plays a dominating role in the production of other climacteric symptoms is responsible for sighing respiration in an unknown way

Sighing respiration is often rapidly abolished by therapy with estrogens The great apprehension and anxiety exhibited by many of those affected has led some observers to regard the symptoms as manifestations of hysteria but specific treatment creates a great change and the distress may vanish in a few days

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Chapter 2

The Size of the Normal Heart

The average weight of the adult heart is 250 grams (females) to 300 grams (males). There is a definite correlation between body weight and the weight of the heart although this correlation is not valid in obesity. The normal heart at birth weighs about 23 grams. The weight of the heart increases in proportion to the weight of the skeletal muscles (a fact known to Harvey). The taller and the heavier a man is, the larger his heart.

Generally speaking, the weight of the heart in man and animals increases with added physical activity. It is small in people engaged in sedentary work but large in athletes and in those who do heavy physical labor.

Position of the Diaphragm. The size and shape of the normal heart varies with the individual; it may even change in the same person within a short time, for it depends upon many factors. The position of the diaphragm, for example, is an influencing factor. A diaphragm too low to afford cardiac support results in a "pendulum" or "vertical" heart. The observer may consider such a heart normal in size even though an enlargement is actually present. If, on the other hand, the diaphragm is elevated, the apex beat may be located outside the mid clavicular line and the mistaken diagnosis of cardiac enlargement may be made.

Figure 6 shows how the heart changes its size and shape when the position of the diaphragm varies. Figure 6a depicts the heart when the diaphragm is high. The heart seems large with a pronounced waist line. The vascular band is wider and an enlargement of the aorta may be erroneously assumed. In Figure 6c (low diaphragm) the cardiac axis is perpendicular, causing the heart to appear small. Figure 6b shows the form of the average normal heart when the diaphragm is in a normal position.

Physical Exertion. After brief but heavy physical exertion the heart may temporarily enlarge, such enlargement lasting for only a few minutes. The subsequent reduction of size may persist for hours or days. The enlarg[illegible] probably due to increased venous return with greater cardiac filling, [illegible] reduction in size can be attributed mainly to the tachycardia which [illegible] diastole (ventricular filling) and to an increase in sympathetic tonus.

After prolonged exertion, cardiac enlargement may be more [illegible] more marked; this is particularly apt to occur when the muscle [illegible]

damaged the individual is unaccustomed to such effort and the exertion is unusually strenuous (Zdansky)

Heart Rate Cardiac rate exerts a marked influence on cardiac size The heart becomes smaller in tachycardias and larger during bradycardias Thus in cases of heart block or in healthy young athletes who develop bradycardia while in training the heart is large In these instances the augmented size is a result of prolonged diastole with greater ventricular filling

Blood Volume The heart becomes smaller after a copious phlebotomy and after diarrhea with dehydration and becomes larger for a few minutes after an intravenous infusion It is very small in patients with Addison s disease particularly during a crisis when there is reduction of blood volume it returns to normal when the crisis is treated successfully (McCavack)

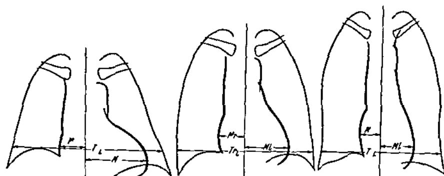


FIG 6 Changes in the shape of the normal heart and of the transverse cardiac diameter in different positions (a) With a high diaphragm (b) normal position of the diaphragm (c) with a low diaphragm (Zdansky)

Measurement Since so many factors exert a marked influence upon cardiac size methods of finding slight enlargement by mensuration of different diameters are fraught with error and may lead to false impressions Moreover such measurements do not permit an unequivocal detection of early cardiac enlargement and they are superfluous when definite changes are present therefore they will not be discussed in detail If measurements are recorded films ought to be obtained when the patient is recumbent since this position allows better filling and minimizes variations Tables have been constructed which predict the cardiac measurements for various heights and weights (Ungerleider) In many conditions e g deformities of the chest pregnancy or ascites mistakes will occur when these tables are used

The cardiothoracic ratio which enjoys considerable popularity is obtained in the following manner The width of the chest is measured at the level of the uppermost portion of the diaphragmatic dome the inner side of the ribs being used as end points The transverse diameter of the heart is considered the sum of the greatest distances between the right and left cardiac borders from the midline (fig 6) The normal ratio between the diameter of the chest and the transverse diameter

of the heart varies with the age and size of the individual but it may be considered 2 1 for the adult male Figure 6 shows how these values depend upon the position of the diaphragm the ratio increases as the diaphragm descends Abnormal values are obtained in patients who are very tall or stocky The cardiothoracic ratio (or cardiopulmonic ratio) therefore furnishes little clinical help in determining early cardiac enlargement Moreover certain parts of the heart may be enlarged even when the transverse diameter is normal (see outflow tract of the right ventricle)

Congestive heart failure may be present with a small heart (in myocardial infarction) and it may be absent with the very large hearts of cor bovinum in hypertension or aortic insufficiency

In patients with scoliosis or funnel chest the heart is often displaced and appears larger than it actually is

That changes of shape often are of greater diagnostic value than changes of size will be evident from the discussion in the succeeding chapters

Tonus of the Heart This phenomenon defies definition We refer the reader to Zdansky s discussion of the problem Many authors believe that tonus is not a separate function of the heart but anyone who sees the flabby almost shapeless heart resting on the diaphragm in certain myocardial diseases and compares it with the heart of normals or of those in good physical condition will be inclined to think otherwise

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Chapter 3

Hypertrophy and Dilatation of Cardiac Chambers

General Discussion

Dilatation of a chamber of the heart often is an occurrence which enables the heart to adapt itself to a changed situation It appears under different conditions

First an increased inflow into the heart (arteriovenous fistula patent ductus arteriosus rapid intravenous infusions) augments cardiac filling and leads to an increased content of blood at the end of diastole As a consequence the myocardial fibers are subjected to greater stretch so that according to the law of Starling a stronger contraction results and the heart is able to cope with the increased demand The dilatation at the end of systole may be minimal This is also the manner in which the left ventricle disposes of increased filling if a mitral or aortic insufficiency is present Within physiological limits the larger the volume of the heart the greater is the energy of its contraction and the amount of chemical change at each contraction The energy of contraction however measured is a function of the length of the muscle fiber (Starling) In addition to the volume at the end of diastole hormonal and neurogenic factors also are influences on cardiac performance

Starling s law of the heart has been questioned lately but has also been confirmed and amplified (Sarnoff)

Second dilatation occurs when the heart works against increased resistance (hypertension aortic stenosis) and is incapable of expelling all of its contents at the end of systole Cardiac output initially diminished soon becomes normal

Third if a primary myocardial lesion or one caused by coronary artery disease renders the muscle unable to contract against the resistance of a normal diastolic blood pressure the amount of residual blood again increases Filling is greater and contraction improves

Hypertrophy develops within a few weeks in such hearts The increased stretch presumably acts as the physiologic stimulus In hypertrophy muscle fibers become larger in rare instances a numeric increase of fibers has been observed (Linzbach)

Hormonal factors in the development of hypertrophy are discussed by Raab

ATRIAL HYPERTROPHY AND DILATATION

Physicians are often confused about the possibility of determining the presence of hypertrophy or dilatation of the atria or the ventricles by physical examination It may be worthwhile therefore to review the subject in a few introductory remarks

Atrial Hypertrophy

Hypertrophy of the right or left atrium even when extreme cannot be detected by physical examination moreover it does not significantly change the shape of the heart on x ray examination The slight dilatation that invariably precedes hypertrophy scarcely exceeds the limits of normal variation Therefore massive hypertrophy of the left atrium in mitral stenosis or of the right atrium in tricuspid stenosis cannot be diagnosed except by inference

Dilatation of the Left Atrium

This occurs in two ways both illustrated by the two lesions which commonly deform the mitral valve In mitral stenosis the atrium can compensate for some time by hypertrophy alone Only when hypertrophy no longer suffices and the atrium cannot expel its contents through the narrowed valve does the retention of larger amounts of residual blood at the end of systole cause dilatation This is called secondary dilatation From the onset of mitral insufficiency however blood enters the atrium both from the pulmonary veins and under high pressure from the left ventricle by regurgitation causing a primary dilatation to appear early

Dilatation of the left atrium may occur mainly along the left cardiac border where it straightens the waist line and causes dullness in the second interspace to the left of the sternal border this is one reason for mitralization of the heart Owing to this enlargement and also to the rotation of the heart to the left (clockwise) in mitral stenosis the left atrium may become visible on the right cardiac border during roentgenologic examination Normally it just reaches this border In some patients with mitral insufficiency and a huge left atrium a very strong pulsation appears at the *right* of the sternum between the fourth and sixth ribs for the atrium fills under high ventricular pressure and may closely approximate the chest wall in this area Marked enlargement of the left atrium may cause left paravertebral dullness between the third and sixth dorsal vertebra We have seen patients with a giant left atrium in whom the left pleura was tapped because of a mistaken diagnosis of pleural effusion

The position of the left atrium as the uppermost posterior part of the heart and its location beneath the tracheal bifurcation in front of the esophagus explains why it displaces these structures when it enlarges Compression of the left main bronchus and displacement of the esophagus occur these actions will be discussed in the chapter on mitral stenosis

Radiologic examination will best reveal dilatation of the left atrium in the early stage if the patient is placed in the right anterior oblique position i e turned 30 to 40 degrees to the left Then the normally clear retrocardiac space is filled by the shadow of the left atrium A study of the course of the esophagus in this position is helpful If the patient swallows a suspension of barium sulfate



Fig 7 Displacement of the esophagus by an enlarged left atrium in mitral stenosis (right anterior oblique position)

the normal esophagus is seen to swerve in a slight arc whose concavity is directed toward the abdomen In left atrial enlargement the esophagus is displaced sharply backward just beneath the bifurcation of the trachea

In figure 7 the typical displacement of the esophagus just beneath the bifurcation of the trachea is clearly visible The picture was obtained in the right anterior oblique position from a patient with rheumatic mitral stenosis and regurgitation

Occasionally a slight circumscribed displacement may occur without left atrial enlargement when the diaphragm is high Therefore the observation should be made during deep inspiration Persistent esophageal displacement in

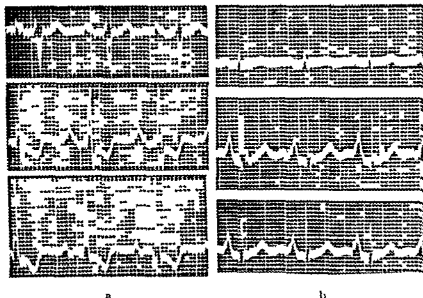
deep inspiration speaks in favor of enlargement of the left atrium A pericardial effusion or an enlargement of the left ventricle causes a similar dorsal displacement of the esophagus this however does not begin just below the bifurcation and is less sharply circumscribed

Dilatation of the Right Atrium

This can be easily demonstrated by percussion since dullness is obtained at the right lower cardiac border and to a variable extent beyond the edge of the lower sternum This enlargement is also readily demonstrated by x ray but it must be differentiated from displacement by an enlarged right (or even left) ventricle Usually such differentiation is possible when the patient is in the oblique position and when an examination is made of the neck veins and the liver Enlargement of the right atrium when extensive is accompanied by hepatomegaly and congestion of the neck veins

Electrocardiogram

The electrocardiogram offers some aid in the differentiation of atrial hypertrophy and dilatation In mitral disease with predominant left atrial dilatation



a b

FIG 8 The three standard leads Figure 8a shows a right ventricular strain pattern and widened slurred P waves in leads I and II in a patient with mitral stenosis figure 8b shows abnormally high P waves in leads II and III in a patient with chronic pulmonary emphysema

abnormally wide slurred and notched P waves appear in leads I and II (figure 8a) This is probably due to intra atrial conduction disturbances associated with marked left atrial dilatation In right atrial hypertrophy as seen in the various types of cor pulmonale the P waves are low in lead I but unusually high often

over 3 mm in leads II and III (figure 8b) These waves are not wide abnormally slurred or notched In this instance hypertrophy of the right atrium seems solely responsible The tall P waves (figure 8b) are followed by depressed P R and RS T segments This is due to the pronounced T waves of the P (Ta or Tp waves)

Very large P waves in all leads are often seen in congenital heart diseases such as the tetralogy of Fallot Occasionally these typical changes of the P waves provide diagnostic help in difficult cases Figure 9 shows the huge P waves in leads I and II obtained from a 4 year old child with tetralogy of Fallot

VENTRICLES

Inflow and Outflow Tracts

Cardiac dilatation and hypertrophy do not develop simultaneously in all parts of the right or left ventricle when these structures are subjected to increased strain The sequence of cardiac dilatation and hypertrophy follows certain rules (Kirch)

Each ventricle may be divided into two parts which function as physiologic units (figure 10) The inflow (receiving) portion is located between the atrio ventricular orifices and the apex while the outflow (expelling) portion is found between the apex and the semilunar valves These sections converge toward the apex The inflow tract of the right (or left) ventricle is represented by the posterior part of the ventricles and adjoining septum whereas the outflow tract is formed by the anterior ventricular wall and adjoining septum When dilatation (and hypertrophy) develop in a healthy right (or left) ventricle owing to an increased pressure in the lesser (or systemic) circulation the only part affected at first is that situated immediately below the semilunar valves (terminal portion of the outflow tract) The dilatation gradually extends toward the apex and only then affects the inflow tract as well Thus dilatation progresses gradually moving from one part to another in a direction opposite to that of blood flow If for some reason the cause of ventricular hypertrophy disappears (left ventricular hyper trophy in hypertension) recovery starts at the end of the inflow section and moves with the blood stream down toward the apex and then up to the arterial orifice This tonogenic dilatation the result of increased resistance causes the heart to enlarge mainly along the longitudinal axis of the outflow tract

These postmortem observations have been confirmed by experiments on the mammalian heart In aortic stenosis the conus area is exposed to increased intraventricular pressure for a longer time and it retains more residual blood than the rest of the ventricle at the end of systole With increasing resistance to the emptying due to an increasing residuum of blood the process gradually extends toward the apex this produces a gradual dilatation in a direction opposite to that of the intracardiac blood stream

In patients with mitral insufficiency the inflow of larger quantities of blood from the atrium to the left ventricle during diastole leads to an early dilatation

of the inflow tract the same process applies to the right ventricle in a tricuspid insufficiency These rules are not applicable to cardiac dilatation resulting from myocardial damage (myogenic dilatation) since here the entire chamber dilates simultaneously This is seen in myocarditis or coronary sclerosis

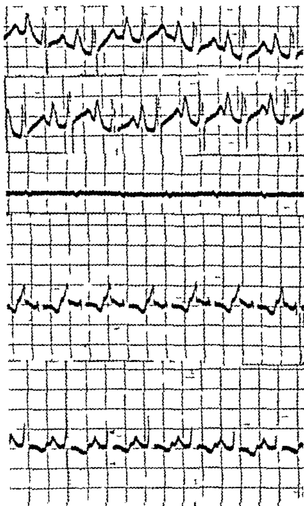


FIG 9 Huge T waves in the standard leads as well as in V 2 and V 5 in a child with Fallot's tetralogy

Involvement of the inflow or outflow tracts of the right ventricle can be recognized fluoroscopically especially in the left anterior oblique position Occasionally important diagnostic data are obtained by this means The inflow tracts of both ventricles are situated posteriorly the outflow tracts anteriorly Hence the most anterior portion of the heart is the outflow tract of the right ventricle (conus of the pulmonary artery) while the most dorsal section is the inflow tract of the left ventricle and the left atrium

In figure 10a b c the positions of the inflow and outflow tracts of the right and left ventricles are indicated by arrows Figure 10a is a postero anterior view Figure 10b shows the right anterior oblique position and figure 10c the left anterior oblique position

It can be seen in figure 10a that the inflow and outflow tracts of the *left* ventricle run almost parallel The inflow tract from the mitral valve to the apex is situated posteriorly and borders on the posterior mediastinum The outflow tract from the apex to the aortic orifice forms the left cardiac border Simple

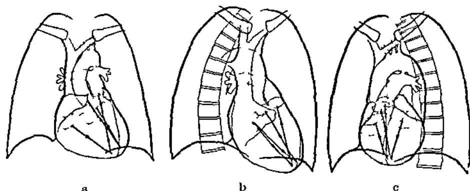


FIG 10 Course of the inflow and outflow tracts of the right and left ventricles (a) postero anterior position (b) right anterior (c) left anterior oblique position (Zdansky)

prolongation of the outflow and inflow tracts along their axes without dilatation along the transverse diameter will displace the apex beat downward but the heart will not appear larger as more of the left ventricle will be hidden in the abdominal shadow than under normal conditions

The inflow tract of the *right* ventricle extends from the tricuspid orifice toward the apex of the right ventricle lying more or less horizontally upon the *diaphragm* *The outflow tract of the right ventricle* on the other hand runs almost perpendicularly upward from the apex to the pulmonary orifice

Dilatation of the inflow tracts is best studied in the left anterior oblique position (figure 10c) for which the patient turns 40 to 60 degrees to the right *If the inflow tract of the left ventricle is dilated a greater part of the left ventricle* is hidden in the shadow of the vertebral column enlargement of the inflow tract of the right ventricle makes the right heart border more prominent so that it bulges into the right lung field

The enlargement of the outflow tract of the right ventricle is best studied in the right anterior oblique position (figure 10b) which brings the prominent conus into view in the postero anterior position it causes filling of the waist line

Hypertrophy of the Left Ventricle

One often hears the remark that the right or left ventricle is hypertrophied because of some particular finding on percussion or x ray examination It may not be amiss to stress that concentric hypertrophy even if massive does not

necessarily alter cardiac size enough for demonstration by percussion Only *one* sign of left ventricular hypertrophy is found on physical examination a heaving strong apical impulse which can scarcely be suppressed by the examining fingers despite the use of considerable force Such a sign however is uncommon The apical impulse is not palpable in the recumbent patient in at least 60 per cent of normal adults *This is to be expected since most of the left ventricle is located* posteriorly the apical area is thoroughly covered by lung and the impulse is absorbed by the chest wall Conditions are not much different when there is hypertrophy of the ventricle Accordingly the apical impulse is heaving only in a minority of cases When this sign is positive it often stems also from displacement of the apex by dilatation of the left ventricle bringing it nearer to the chest wall Hypertension or aortic stenosis may persist for years and hypertrophy of the left ventricle may reach great proportions without there being any evidence from physical examination to prove the existence of this hypertrophy Usually the presence of *hypertrophy is merely inferred* its existence cannot *be positively* demonstrated

The situation *is somewhat similar on x ray examination Only* greater rounding of the lower left cardiac border and apical area is found but this finding is also noted in normal hearts and in athletes In concentric hypertrophy of the left ventricle for a long time only the outflow tract — which is not very accessible to examination — is involved Hypertrophy of the left ventricle need not necessarily be accompanied by a similar change in the right ventricle

The electrocardiogram is discussed below

Hypertrophy of the Right Ventricle

Hypertrophy of the right ventricle can be demonstrated more readily The right ventricle lies anteriorly immediately behind that part of the thoracic wall called the precordium In this area the lung either *does not cover the heart* or covers it only in part and thus right ventricular hypertrophy causes a diffuse and increased pulsation of the whole area to the left of the lower sternum The most anterior part of the heart is the outflow tract of the right ventricle that is the conus of this ventricle Since in the majority of cases it undergoes hypertrophy first a pulsation of the conus area is palpable very early

It is in cases of pulmonary emphysema and abnormalities of the thoracic wall that the pulsation does not appear The sign is not pathognomonic however since it is found in the absence of right ventricular hypertrophy i e in the juvenile heart *when the chest* wall is thin and *in the overactive heart of cardiac neurosis* hyperthyroidism or avitaminosis (beriberi heart) The differential diagnosis is nevertheless usually easy

Pure hypertrophy of the right ventricle without dilatation is difficult to detect by x ray When the conus of the right ventricle is accentuated and the right ventricular contour is more prominent in the left anterior oblique position dilatation of considerable degree has already taken place

The electrocardiogram is discussed below

during systole if the amount of fluid in the alveoli is greater than normal (cardio pulmonic rales) In cases of marked ventricular hypertrophy and dilatation a larger part of the heart is close to the anterior chest wall and the lung having lost its elasticity due to chronic congestion cannot expand with sufficient speed during cardiac systole Therefore the atmospheric pressure presses on the soft inter spaces and causes systolic retractions — which are so often misinterpreted as being caused by pericardial adhesions

Right ventricular dilatation usually involves the outflow tract primarily (tonogenic dilatation) the conus area therefore shows the first evidence of en largement The axis of the outflow tract of the right ventricle is almost perpen dicular (figure 10a) Upward dilatation develops easily whereas the diaphragm prevents downward expansion Therefore a prominent conus of the right ventricle in the right oblique position and mitralization in the postero anterior position are early roentgenologic signs of right ventricular dilatation The enlarged conus of the right ventricle is best visualized when the patient is standing in a lordotic position

Dilatation of the inflow tract of the right ventricle e g in a tricuspid regur gitation causes a marked enlargement of the cardiac shadow to the right and left since the axis of the inflow tract of the right ventricle runs almost horizon tally from right to left

Electrocardiogram

The electrocardiogram may be normal despite the presence of cardiac hyper trophy and dilatation In more advanced hypertrophy and dilatation of a ven tricle the electrocardiogram assumes a typical pattern The presence or absence of an axis deviation which was strongly emphasized a few years ago is of little importance In patients with left ventricular hypertrophy but a perpendicular cardiac axis no left axis deviation need be present while in right ventricular hypertrophy and a horizontal heart left axis deviation has been seen *Thus the position of the heart is of importance for the appearance of an axis deviation* If a marked emphysema supervenes in a patient with left ventricular hyper trophy due to hypertension and the heart assumes a more perpendicular position the two factors (hypertrophy and position) acting in opposite directions may cause the disappearance of any deviation or even the appearance of a right axis deviation In left ventricular hypertrophy occasionally the QRS complexes are 0 10 or 0 11 second wide The PS T segments and T waves are displaced in the standard leads in a direction opposite to the QRS complexes

The chest leads are of greater importance than the standard leads for the diagnosis of hypertrophy As figure 13 shows in left ventricular hypertrophy the P wave in V 2 may become lower or may disappear while the S wave is deeper The RS T segment is often more elevated than in normal hearts In V 6 the P wave is very large the S wave is often absent and the PS T segment as well as the T waves are depressed below the zero line as in lead I In right ventricular

necessarily alter cardiac size enough for demonstration by percussion Only *one* sign of left ventricular hypertrophy is found on physical examination a heaving, strong apical impulse which can scarcely be suppressed by the examining fingers despite the use of considerable force Such a sign however, is uncommon The apical impulse is not palpable in the recumbent patient in at least 80 per cent of normal adults This is to be expected since most of the left ventricle is located posteriorly the apical area is thoroughly covered by lung and the impulse is absorbed by the chest wall Conditions are not much different when there is hypertrophy of the ventricle Accordingly the apical impulse is heaving only in a minority of cases When this sign is positive it often stems also from displacement of the apex by dilatation of the left ventricle bringing it nearer to the chest wall Hypertension or aortic stenosis may persist for years and hypertrophy of the left ventricle may reach great proportions without there being any evidence from physical examination to prove the existence of this hypertrophy Usually the presence of hypertrophy is merely inferred its existence cannot be positively demonstrated

The situation is somewhat similar on x ray examination Only greater rounding of the lower left cardiac border and apical area is found but this finding is also noted in normal hearts and in athletes In concentric hypertrophy of the left ventricle for a long time only the outflow tract — which is not very accessible to examination — is involved Hypertrophy of the left ventricle need not necessarily be accompanied by a similar change in the right ventricle

The electrocardiogram is discussed below

Hypertrophy of the Right Ventricle

Hypertrophy of the right ventricle can be demonstrated more readily The right ventricle lies anteriorly immediately behind that part of the thoracic wall called the precordium In this area the lung either does not cover the heart or covers it only in part and thus right ventricular hypertrophy causes a diffuse and increased pulsation of the whole area to the left of the lower sternum The most anterior part of the heart is the outflow tract of the right ventricle that is the conus of this ventricle Since in the majority of cases it undergoes hypertrophy first a pulsation of the conus area is palpable very early

It is in cases of pulmonary emphysema and abnormalities of the thoracic wall that the pulsation does not appear The sign is not pathognomonic however since it is found in the absence of right ventricular hypertrophy i e in the juvenile heart when the chest wall is thin and in the overactive heart of cardiac neurosis hyperthyroidism or avitaminosis (beriberi heart) The differential diagnosis is nevertheless usually easy

Pure hypertrophy of the right ventricle without dilatation is difficult to detect by x ray When the conus of the right ventricle is accentuated and the right ventricular contour is more prominent in the left anterior oblique position dilatation of considerable degree has already taken place

The electrocardiogram is discussed below

Dilatation of Left and Right Ventricle

Dilatation of the left or right ventricle increases the size of the heart and therefore cardiac enlargement is found on percussion or by x ray examination *Since both ventricles are situated mainly in the left chest it is often impossible* to decide by percussion alone which ventricle is enlarged

Left Ventricle The position of the apical impulse if present permits one to deduce which ventricle is dilated The normal apical impulse is located in the fifth left intercostal space within the mid clavicular line Dilatation of the left



FIG 11 Displacement of the apex beat with dilatation of the left (a) and of the right (b) ventricle

ventricle displaces the apex beat outward and *downward* in the direction of the arrow in figure 11a The left leaf of the diaphragm is often pushed downward When the outflow tract of the left ventricle dilates e g in hypertension or aortic valve stenosis the expansion occurs almost exclusively along the axis of the outflow tract (figure 10a) If there is no widening along the transverse diameters percussion and fluoroscopy will fail to disclose much cardiac enlargement in the usual sense The heart merely becomes oblong (egg shaped) and as pointed out before a greater part of the enlarged ventricle is hidden in the abdominal shadow This part becomes visible only if a large amount of gas is present in the colon or stomach

In myocardial lesions and in more advanced stages of left ventricular dilatation the inflow tract becomes involved the heart enlarges along the transverse axis and the characteristic aortic configuration appears

Right Ventricle With right ventricular dilatation the apex beat is displaced mainly outward but not downward (figure 11b) Often it is situated a little higher than the normal location and an epigastric pulsation is frequently present

Since the right ventricle is located anteriorly the occurrence of hypertrophy and dilatation of this chamber in childhood (before the chest develops fully) *causes a characteristic bulge of the precordium The left mammilla therefore may* have a different position than the right one

Figure 12 shows a characteristic bulge over the precordium in a patient who developed rheumatic mitral stenosis and regurgitation in early childhood Pronounced hypertrophy and dilatation of the right ventricle were present

Right ventricular dilatation may also cause a diffuse systolic retraction of the interspaces in the precordial area. Normally when the ventricles contract the



Fig 1 Bulge of the precordial area of the chest wall in a patient with a rheumatic mitral stenosis and regurgitation

negative intrathoracic pressure increases because blood leaves the chest; the elastic lung bordering on the heart immediately widens and fills the gap (Lang). This explains why moist rales are heard over the anterior part of the left lung

during systole if the amount of fluid in the alveoli is greater than normal (cardio pulmonic rales) In cases of right ventricular hypertrophy and dilatation a larger part of the heart is close to the anterior chest wall and the lung having lost its *elasticity due to chronic congestion cannot expand with sufficient speed during* cardiac systole Therefore the atmospheric pressure presses on the soft inter spaces and causes systolic retractions — which are so often misinterpreted as *being caused by pericardial adhesions*

Right ventricular dilatation usually involves the outflow tract primarily (tonogenic dilatation) the conus area therefore shows the first evidence of en largement *The axis of the outflow tract of the right ventricle is almost perpen* dicular (figure 10a) Upward dilatation develops easily whereas the diaphragm prevents downward expansion Therefore a prominent conus of the right ventricle *in the right oblique position and nitralization in the postero anterior position* are early roentgenologic signs of right ventricular dilatation The enlarged conus of the right ventricle is best visualized when the patient is standing in a lordotic *position*

Dilatation of the inflow tract of the right ventricle e g in a tricuspid regur gitation causes a marked enlargement of the cardiac shadow to the right and *left since the axis of the inflow tract of the right ventricle runs almost horizon* tally from right to left

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hypertrophy the R wave in V2 is often but not invariably taller than usual and the T wave is flat or inverted In V5 there are deep S waves preceded by R waves of medium height The RS T segments and T waves are normal in V5

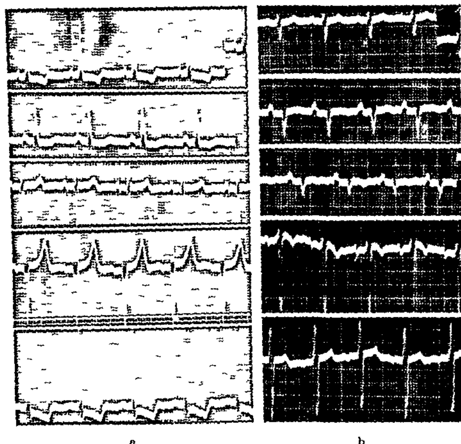


Fig 13 Electrocardiograms showing the patterns of left (a) and right (b) ventricular hypertrophy Figure 13a was registered from a 68 year old woman with hypertension figure 13b was obtained from a 58 year old patient with pulmonary emphysema

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Chapter 4

Percussion and Auscultation

Percussion

Introduction

In recent years with the development and increased availability of roentgenology percussion of the cardiac borders is hardly taught or practiced in many institutions It has been called a dying method which served in the past but should be extruded from our important and growing number of clinical and laboratory methods (Parkinson) One must concede that roentgenology and especially fluoroscopy give more exact and more detailed information about the size and what is more important the shape of the heart Moreover patients with emphysema obesity or a deep or deformed thorax (kyphoscoliosis) present unsurmountable obstacles to cardiac percussion Furthermore in such cases percussion often provides misleading information Notwithstanding the fact that moderate emphysema is not rare in cardiac patients percussion is and will continue to be however a very important and valuable method for every student and physician so long as x ray machines will not fit into the doctor s bag Those who ridicule percussion or deny the possibility of obtaining information from it deprive themselves of a valuable means of learning at the bedside the size and shape of the heart

Technic

As an aid to reliable and informative cardiac percussion one should mark the borders of the heart as obtained by percussion with a skin pencil (dermatograph) and try to locate the right and left borders This *orthopercussion* provides information about the size and shape of the heart and furnishes results that can be compared in accuracy to those of a postero anterior x ray film

It is well to percuss first the attachment of the right diaphragm or the lower border of the right pleural sinus for percussion of the dome of the diaphragm is unreliable In about 67 per cent of normal adults small dilated cutaneous veins (pleural sinus veins) indicate the site of the pleural sinuses The presence of these veins does not indicate pulmonary cardiac pleural or hepatic pathology as is often suggested Rather the veins are physiologic structures most obvious in those engaged in athletics or heavy physical work (Burrett and Scherf) and are more pronounced in patients with an obstruction of the superior vena cava Figure 14

shows very pronounced pleural sinus veins in a patient with a mediastinal tumor (lymphosarcoma) Smaller chains of veins are seen in normals



FIG 14 Pleural sinus veins in a patient with a mediastinal tumor

After determining the border between the lowest part of the lung and liver which can be obtained with very light percussion the right border of the heart is mapped out Percussion is performed in the interspaces from right to left In mapping out the left cardiac border one starts at the second interspace When the

lower half of the left cardiac border is reached the examiner attempts to keep the plessimeter finger parallel to it and disregards the interspaces

One question arises very often Should the first suggestion of diminished resonance or a very distinct dullness be considered as the cardiac border? If the former is used and the heart is enlarged impairment will be found at some distance from the heart On the other hand very light percussion obtains the area of absolute dullness this shows only how much of the heart is uncovered by lung and *yields little information about cardiac size and shape For the best results* the beginner should mark the border at points where the difference between two successive percussion strokes is most distinct

The examiner should never draw a line upon the discovery of a dull area but instead should mark it with a dot In this way the subjective aspect of percussion is reduced

Experience gained in the instruction of many groups of undergraduate students in physical diagnosis has shown the inadvisability of giving general or specific rules concerning the force used in percussing different parts of the right or left borders Such rules confuse rather than help the beginner Practice alone provides the necessary experience and makes it possible to consider such numerous variables as the shape of the thorax the amount of subcutaneous fat the resonance of the thoracic cage etc

To avoid errors created by diaphragmatic elevation and to obtain sharper dullness percussion should be performed whenever possible with the patient standing In this position the heart approaches the anterior chest wall so that the changes on percussion are clearer and more distinct When percussion is performed on a bedridden patient right handed individuals should always stand on the left side since otherwise the plessimeter finger could not be kept parallel to the cardiac border

Patients with a high diaphragm as well as those with right ventricular dilatation often have a definite dullness at the lower sternum

Much more important than the determination of the transverse diameter of the heart either by percussion or x ray examination is the establishment of the cardiac shape Thus in enlargement of the outflow tract of the right ventricle the heart assumes a mitral shape i e filling of the waist line This derives from *the almost perpendicular position of the outflow* tract of the right ventricle The transverse diameter of the heart may be normal In enlargement of the outflow tract of the left ventricle displacement of the apex beat downward and outward *is of diagnostic value here as well the transverse diameter of the heart may* be normal

Right Cardiac Border

The lower half of the right border is formed by the right atrium (figure 10a) Rarely the right ventricle contributes a very short section to the lowest portion of the right cardiac border just above the diaphragm Here the inferior vena cava and the hepatic veins may become visible on x ray with a low position of the

diaphragm The upper half of the right cardiac border is formed by the superior vena cava and the innominate vein but these structures do not play an important role in percussion In many normal subjects particularly in elderly people the ascending aorta participates in the formation of the right cardiac border

On x ray examination the atrial portion of the right border i e approximately the lower half extends about twice as far beyond the vertebral column as the upper half of the cardiac border The dullness produced by percussion of the right lower border under normal conditions projects no more than 5 mm beyond the right edge of the sternum this value may be greater in patients with a high diaphragm

Any dullness beyond this limit in the region of the right lower cardiac border often means enlargement of the right atrium especially when the dullness is clear and superficial Roentgenologically dilatation of the left atrium may cause the right border to protrude farther Enlargement of the right or the left ventricle may also displace the right atrium to the right In hydrothorax percussion of the border of the right atrium is performed most satisfactorily with the patient in the recumbent position for the effusion if not too extensive moves posteriorly in such cases percussion sometimes yields better results than roentgenography

Dullness to the right of the upper half of the right sternal border for all practical purposes and insofar as cardiovascular alterations are concerned always stems from an abnormality of the ascending aorta Normally the aorta is not sufficiently wide or sufficiently superficial to provoke any dullness at this area Dilatation and elongation of the aorta forces the vessel to approach the upper sternum and increases dullness over the manubrium sterni

Left Cardiac Border

The left border of the heart may be divided into four parts formed from above downward by the aortic knob the pulmonary artery the left atrium and the left ventricle (figure 10a) The aortic knob which is formed by the sagittal portion of the transverse aorta is absent in infants and children since they do not have any sagittal section (the aorta proceeds diagonally from the right anterior part of the chest to the left posterior aspects) Percussion of this area is not informative because of the deep position of the aorta

Normally percussion reveals no dullness over the pulmonary artery and the left atrium Only a very small section of the left atrium the tip of its appendix participates in the formation of the left cardiac border The mass of the left atrium is located dorsad Under normal conditions one can percuss in the second and third left intercostal spaces from the axilla to the sternal border without encountering dullness This segment of the left border is called the waistline of the heart

Under physiologic conditions a small portion of the left cardiac border above the appendix of the left atrium is formed by the pulmonary artery The remaining and major part of the left cardiac border swinging in a long arc to the cardiac

apex is formed by the outflow tract of the left ventricle, which also represents the apex. Most of the left ventricle is situated dorsad. The right ventricle lies just under the chest wall anteriorly and does not contribute to the formation of the normal left cardiac border.

Dilatation of the descending aorta cannot be discovered by percussion of the anterior chest wall. *Occasionally, dorsal percussion to the left of the spinal* column elicits some dullness if the descending aorta is dilated.

Mitral Configuration

Enlargement of the conus area (outflow tract) of the right ventricle, as well as dilatation of the pulmonary artery and the left atrium, provoke an easily detected dullness at the second and third left intercostal spaces near the sternum. Thus, the waistline of the heart straightens and one speaks of "mitral configuration" of the heart. Since the discovery of parasternal dullness in the second left intercostal space *readily permits the diagnosis of increased tension in the* lesser circulation, it has great clinical significance.

The term "mitral configuration" is only descriptive and indicates more or less complete disappearance of the waistline; it does not prove the existence of a mitral lesion. Mitralization is absent in early stages of mitral disease; on the other hand, it may be pronounced without presence of mitral disease, e. g., in hypertensive heart disease or in aortic valvular lesions when there is back pressure and hypertension in the lesser circuit. Sometimes, under these circumstances, a relative mitral insufficiency may also contribute to the development of mitralization. Mitralization is common in cor pulmonale.

The individual components of the left heart border cannot be distinguished *in infants and children, for their hearts normally show "mitral configuration"* with a relatively straight left cardiac border. The heart is globular in form. If an adult has a high diaphragm which shoves the heart upward in the midline, the waistline may disappear, creating mitralization. Since this often happens in women, the term "female heart" has gained some currency. Mitralization is also found when the low diaphragm fails to support the heart from below, causing the left border to straighten (figure 6c). Mitralization is also seen sometimes when the right diaphragm is unusually high, and it is common in kyphoscoliosis. In all these instances fluoroscopic study of the heart in oblique positions usually permits the examiner to decide whether an enlargement of the outflow tract of the right ventricle or dilatation of the left atrium causes the mitralization.

Aortic Configuration

*If the left ventricle alone is enlarged, the cardiac waistline becomes accen*tuated, resulting in a condition called "aortic configuration" of the heart. Usually *this change of shape can easily be detected by percussion.* Aortic configuration signifies nothing more than a sharper angle on the left heart border with a large *left ventricle; it does not mean aortic disease.* Since it is present whenever the

left ventricle dilates it is a common finding in certain stages of hypertensive cardiovascular disease in diseases of the aortic valves and in myocardial lesions If a patient has a high diaphragm the apical area of the heart may be displaced upward and to the left to cause an aortic configuration this is often wrongly attributed to an enlarged left ventricle (figure 6a)

Fat Pad

In fluoroscopy and in chest films the lower left border of the heart often seems elongated so that its lowest part exhibits a concavity or (sometimes in inspiration) a convexity outwardly directed This is caused by an accumulation of fat (Fett buerzel) between the layers of the parietal pericardium and the mediastinal pleura (Schwarz) The presence of this fat pad is not restricted to obese people It is usually less dense than the heart is at the apical area Occasionally a fat pad found at the lower right cardiac border is confused with a tumor or a diverticulum

Concluding Remarks

Despite the limitations that emphysema or chest deformities impose upon percussion the method is very useful for discovering dilatation of the heart to the right Moreover percussion is valuable for detecting mitralization especially when the latter *stems from enlargement of the outflow tract of the right ventricle* This tract is located ventrad and produces marked dullness in the second left intercostal space parasternally The aortic configuration in the lesions enumerated above is easily percussed

It will be shown in the chapter on pericardial diseases that percussion is also of major importance in the discovery of a pericardial effusion

Details of percussion and of changes in cardiac shape will be discussed in connection with the individual cardiac lesions

AUSCULTATION

At birth the heart rate is about 180 beats per minute but falls considerably in the following hours

It may be said that normal cardiac action leads to the appearance of four sounds all of which are occasionally audible They will not be described here in the order of their appearance to avoid confusion we shall begin with the classical first heart sound

(1) The *first* heart sound is composed for the most part of vibrations caused by closure of the mitral and tricuspid valves To what extent vibrations caused by the contraction of ventricular muscle are a factor is still a matter of controversy (Dock) The opening of the semilunar valves the vibrations caused by atrial systole and the distension of the ascending aorta and proximal part of the pulmonary artery at the beginning of systole may contribute but certainly only to a small degree The first heart sound appears approximately 0 02 second after the beginning of the QRS complex in the electrocardiogram and lasts between 0 14 and 0 16 second in the phonocardiogram Its loudness — as we shall see —

depends upon the position of the atrioventricular valves at the beginning of systole and upon the anatomic condition of these valves it is louder in anemia

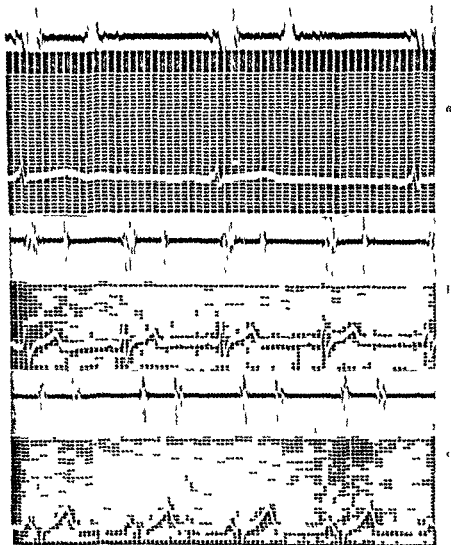


FIG 15 (a) The phonocardiogram and electrocardiogram (lead II) obtained over the cardiac apex from a 22 year old without evidence of cardiovascular disease the vibrations of the loud first heart sound are preceded by coarse vibrations caused by atrial systole there is a faint systolic apical murmur slow and low vibrations of the third heart sound follow those caused by the second sound Figure 15b and c were obtained from a 15 year old male with the microphone over the apical area and over the second left intercostal space parasternally In (b) the first heart sound reveals two groups of vibrations in (c) the second pulmonic sound is split

cardiac neurosis hyperthyroidism fever and mitral stenosis In the phonocardiogram two chief groups of vibrations can be discerned (figure 15a)

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impact murmur which occurs when a jet of blood strikes a part of a vessel a false tendon or a section of a cardiac chamber at a certain distance (Bondi)

False tendons and some aortic insufficiencies cause cooing murmurs like the cooing of a dove or the cry of a seagull These murmurs show regular vibrations *in the phonocardiogram*

The murmurs heard in healthy subjects will be discussed in detail in the section on mitral insufficiency It may be noted by way of anticipation that they are always systolic are most common in young people but also appear in adults particularly when *the velocity of blood flow is increased They are said to be dif* ferent in loudness and to disappear with a change of posture this however is not unusual in murmurs caused by organic heart disease They are also said to change their *loudness with deep inspiration or expiration* Such change is rare with murmurs caused by organic heart disease but since it also takes place in normal persons it cannot be used for a differential diagnosis

The system of grading murmurs introduced by Levine is useful A grade 1 murmur *is one which is just audible while a grade 6 murmur is so intense that it* can be heard without a stethoscope at a distance from the chest wall Grade 5 murmurs are the loudest heard with the stethoscope on the chest but are not audible at a distance Grade 2 murmurs are soft but easily heard From this it will be easy to judge grade 3 (loud murmur) and grade 4 murmur (very loud) so that in actual practice different observers grade murmurs accurately Murmurs from grade 3 to 6 are said never to be found in healthy subjects We would like *to modify this statement to the effect that organic disease is usually present* when such murmurs are heard On the other hand it must be stressed that grade 1 and 2 murmurs may be encountered in people with organic heart disease such as *mitral regurgitation*

Some murmurs e g of mitral stenosis an interventricular septal defect and a patent ductus arteriosus are almost characteristic They are rarely found in other lesions and then other signs permit the differentiation

Murmurs are not always heard best over the auscultation area of the valve from which they originate Diastolic murmurs of aortic regurgitation are often heard over the lower left sternal border A systolic murmur caused by aortic stenosis may be detected only over the apex if emphysema prevents its appear ance in the second right intercostal space These and other related findings will be discussed in detail in appropriate sections

Phonocardiography

With respect to the murmurs that appear in the heart the human ear is an imperfect instrument Vibrations of 20 or less per second are not audible but such vibrations and even those as low as 15 per second occur *in mitral stenosis High pitched sounds may occasionally obscure low pitched ones* Phonocardiography which is almost as old as electrocardiography can often assist in detecting

abnormal vibrations moreover it keeps a documentary objective record of the auscultatory findings Although a less subjective method than auscultation it rarely contributes to the diagnosis based on the existence of murmurs It does aid however in the analysis and differentiation of split sounds gallop rhythms and abnormal clicks

The phonocardiogram may be obtained with three different types of micro phones (1) the linear microphone which magnifies all vibrations uniformly and reproduces particularly well the very low frequency vibrations which nor mally are not heard (2) the stethoscopic microphone which does not reproduce the low vibrations due to the apex beat and the like (these have no value in clinical auscultation) but which magnifies the others to the degree they would be heard were our ear a more perfect instrument and (3) the logarhythmic micro phone which attenuates low frequency vibrations but increases those heard by the human ear on a logarhythmic scale Because of the excessive amplification the linear microphone method is not practical The stethoscopic microphone yields more than just auscultation alone and is best used in clinical studies while the logarhythmic microphone records high pitched vibrations well and is most practical in the verification of clinical impressions

Practical Advice

Auscultation should be performed with the patient in the upright and in the recumbent position Some murmurs such as the diastolic murmurs of aortic valve insufficiency are more audible when the patient stands while mitral mur murs especially those of mitral stenosis are heard better or exclusively when the patient is recumbent Sometimes the latter murmurs are detected only when the patient is lying on his left side Whenever possible the heart should also be auscultated after exertion Some murmurs like the low pitched ones of mitral stenosis are confused with split heart sounds Such a mistake is understandable since from the standpoint of the physicist the physiologic heart sounds are in reality murmurs The French are more nearly correct when they speak of the first and second bruit of the normal heart

For high pitched murmurs a stethoscope possessing a diaphragm chest piece should be used the diaphragm filters low pitched vibrations while the bell receiver facilitates the discovery of low pitched murmurs The ear pieces of the stethoscope should fit well into the auditory canal of the examiner and both should run in the same direction

The most difficult task for beginners is the differentiation of the heart sounds With a normal rate or bradycardia it is easy to determine which sound is the first and which the second but with a tachycardia this task becomes more diffi cult unless the apex beat or carotid pulse is palpated simultaneously Therefore beginners should never listen to the heart without simultaneously palpating the carotid pulse All auscultatory phenomena synchronous with the carotid pulse are systolic Palpatory or auscultatory signs before or after this are diastolic

Many mistakes would be avoided if auscultation were regularly done with one finger resting on the carotid artery

Since details about auscultation are presented in other chapters only a few general facts will be mentioned at this time

Modification of Sounds

The first heart sound is accentuated more often as the result of hyperexcitability of the heart than of organic cardiac disease Frequently very distant and faint sounds suggest pulmonary emphysema rather than myocardial weakness With a few noteworthy exceptions which are discussed elsewhere no conclusions should be drawn concerning the state of the myocardium from the loudness of the heart sounds Subsequently it will be shown that the first or second sound may become accentuated or disappear in a host of conditions even in the absence of intrinsic cardiac damage

Impurity or splitting of the first or second heart sounds are common findings in healthy individuals and particularly in young people On the other hand they are frequently due to cardiac abnormalities The difference in time between the two parts must be at least 0 06 second in order to be perceptible (Lausada) In rare instances splitting is heard when the interval is only 0 03 second

Splitting of the first heart sound is heard best during expiration and at the apex in a healthy person It is ascribed to asynchronous closure of the mitral and tricuspid valves This splitting is not rare in the hyperexcitable heart of cardiac neurosis hyperthyroidism the hypertrophic heart of kyphoscoliosis or fibrotic pulmonary tuberculosis It may be caused by the vibrations of atrial contraction It causes confusion with the murmur of a mitral stenosis Splitting of the first sound may be confused with a presystolic gallop rhythm and a systolic click in pulmonary hypertension or in pericardial adhesions

Systolic clicks will be discussed in the section on gallop rhythm

Duplication of the second heart sound heard best in the second left intercostal space is believed to result from a short difference in time between the closure of the aortic and pulmonic valves (figure 15c) The first part originates in the aortic the second in the pulmonary valves Paradoxical splitting of the second heart sound in which the aortic component appears after the pulmonary one is seen in left bundle branch block and in aortic stenosis It is explained by prolongation of the duration of systole of the left ventricle (Gray)

The phenomenon is heard best and often exclusively over the pulmonary artery in the second left intercostal space and the question arises whether asynchronous closure of the pulmonary valves alone is responsible With the artificial ball valve of Hufnagel for surgical treatment of aortic regurgitation splitting of the second sound may be found (McKusick et al) and may appear when the ball strikes one corner of the orifice before the other This splitting occurs particularly at the end of inspiration and the onset of expiration It is absent in complete pulmonary stenosis and is especially pronounced in right bundle branch block (figure 16)

In a large percentage of children and healthy adults during rest (but some times only on exertion) the third heart sound is heard physiologically over the lower end of the sternum and at the apex In some individuals this low pitched sound is very loud but in others it is scarcely audible It may appear and disappear with the different phases of respiration About 95 per cent of healthy children have a physiologic third heart sound (Steinberg) and it has been observed in 42 per cent of medical students Thayer found a third heart sound in 65 per cent of his normal subjects We occasionally found it during routine examinations in

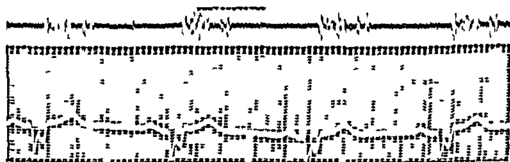


FIG 16 Right bundle branch block (lead II) The phonocardiogram was recorded with the microphone in the second left intercostal space It shows splitting of the second sound

individuals up to but not beyond 25 years of age Some claim to have heard it in normal people as old as 40 It is easily confused with gallop rhythm This triple heart rhythm is best heard in and median to the apical area It may be missed in the erect posture

Some investigators explain that the third heart sound derives from a stretching of the myocardium during the diastolic inflow of blood while others believe that normal filling causes a sound produced by the impact of the ventricles on surrounding tissues But this theory does not explain the fact that the third heart sound can also be heard in the exposed heart It is more probable that the stretching of the fibrous tissue in the chordae tendineae or vibrations of the valves (Lewis and Dock) causes the third heart sound at the beginning of diastole Increasing thickness of the chest wall or in the opinion of others the gradual reduction of cardiac elasticity with increasing age makes the third heart sound disappear

On the small normal chest of children without heart disease but with cardiac hypermotility and more often in children and adults with enlarged hearts a soft grating systolic friction rub is heard The rub may be noted in systole as well as in diastole and it may disappear on deep inspiration This phenomenon results from friction created when the normal epicardium rubs against the normal parietal pericardium It is most frequently detected in hypertensive patients with large left ventricles when they are in the left lateral recumbent position Usually this friction sound is transient It is often noted in connection with the hyperexcitable heart of hyperthyroidism (Goodall) and in this instance it may be

limited to the area over the conus of the pulmonary artery i e the most prominent part of the heart The evaluation of all the clinical data usually permits the differentiation from the friction rub caused by pericarditis

Pulmocardiac murmurs or respiratory heart murmurs are heard most commonly along the left cardiac border They are explained by pulmonary compression when the heart enlarges in diastole or by pulmonary expansion when the heart becomes smaller in systole since air may be thus expelled or drawn into a section of lung thereby producing rales or a murmur Ordinarily a little experience will permit differentiation from an endocardial murmur Naturally these phenomena are more frequent when the heart is enlarged They are heard best over the lingula of the lung near the conus of the pulmonary artery In this area rales are often audible in one or the other phases of the cardiac cycle (cardiopulmonic rales)

More often in children but occasionally in adults particularly with anemia a venous hum may be heard over the base of the heart transmitted from the large veins of the supraclavicular area The hum is continuous and shows a diastolic accentuation since blood flows faster in the veins in ventricular diastole This murmur is mentioned in the chapter on aortic insufficiency and anemia

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Chapter 5

Compensation and Decompensation

Cardiac Reserve and Compensation

A fundamental property of heart muscle is an ability to accommodate its activity to the requirements of the organism This adaptibility is what makes life possible since it permits the heart to increase its stroke and minute volumes and thus meet greater demands of the body during exertion digestion pregnancy and innumerable other situations The amount of blood expelled by the heart may increase from 5 to 7 liters per minute at rest to 25 or 30 liters during vigorous exercise The myocardium does not utilize all its potentialities during rest a reserve force is available and is brought into play whenever the filling of the heart increases Within certain limits Starling s law can be applied to the healthy heart i e greater stretching of the myocardial fibers by increased cardiac filling causes a stronger contraction

During exertion large amounts of blood are returned rapidly from the muscles and blood depots to the right heart so that its contents increase The left heart thus receives and expels more blood and the output per minute rises In some patients an increase of blood pressure offers added resistance to the discharge from the left ventricle which does not empty completely for a few beats This increases the amount of residual intraventricular blood at the end of systole slightly distends the left ventricle and stretches the cardiac muscle fibers thus systole becomes stronger even when the inflow from the atrium remains constant After a few beats cardiac output is the same as before the elevation of blood pressure

Under physiologic conditions the output of the heart per minute can be increased in another simple manner namely by acceleration of cardiac rate If the tachycardia does not exceed certain limits (about 120 beats per minute) the diastolic filling is not impaired and therefore the output per minute of the heart will be markedly increased

Under pathologic conditions the heart endeavors to adapt itself as we shall see to the changed situation by means of similar mechanisms i e it attempts to compensate for the consequences of the disease If the heart succeeds in supplying an adequate amount of blood to every part of the body so that sufficient quantities of oxygen reach all tissues while metabolites like carbon dioxide are speedily removed and congestion is avoided one speaks of a compensated circulation The chief goal of compensation is to deliver a normal minute volume not

only at rest but also when demands are moderately increased If the cardiac reserve is decidedly diminished with the result that the circulation is adequate only at rest or with very restricted effort such as walking on level ground while ascent of stairs causes distress the condition borders on decompensation If the faltering heart can no longer accomplish its tasks and symptoms perhaps trifling at first gradually or suddenly become worse one speaks of failing or broken compensation or decompensation The term congestive heart failure is also employed when the circulation is no longer adequate and passive congestion (increased venous pressure in the lesser or systemic circulation) is present even during rest To be sure the concept of decompensation is rather hazy which accounts for the bewildering variety of definitions that have been advanced

BACKWARD AND FORWARD FAILURE

The mechanism of cardiac failure has interested physicians for more than a century The theory that the cavity behind the failing one suffers first — an idea propounded by Hope as early as 1842 — was widely accepted and subsequently supported by Starling s experiments Blood dams up behind the failing ventricle Thus with insufficient systolic emptying of the right ventricle the amount of residual blood at the end of systole is increased the diastolic pressure in the right ventricle is higher and the normal inflow of blood from the right atrium is impeded the pressure in the right atrium rises until an effective pressure gradient is re established causing increased venous pressure With failure of the left ventricle similar changes occur in the left atrium and the lesser circuit All this leads to a diminished cardiac output In order to maintain a normal blood pressure a reflex arteriolar constriction occurs This causes peripheral hypoxia and stimulates the bone marrow Blood volume increases (Starling)

This back pressure theory is still valid Early voices were raised however pointing out that some phenomena particularly paroxysmal dyspnea in cardiac patients are better explained by the diminished output of the failing heart (forward failure theory) With the introduction of cardiac catheterization and the possibility of determining cardiac output with greater accuracy the occurrence of a diminished output in patients with a failing left ventricle as the result of hypertension coronary sclerosis or aortic valvular lesions was confirmed These investigations and the determination of the renal blood flow (see below) induced many physicians to explain all signs of heart failure by forward failure According to this conception ventricular failure and the ensuing diminution of cardiac output lead to a reduced blood supply to the kidney causing diminished excretion of sodium and water The increase in blood volume is the reason for the elevated venous pressure For many practitioners the old concept of backward failure was a thing of the past and the new theory was believed to be the only one to explain all signs of heart failure

Critical evaluation of the data obtained in the laboratory and clinical observations in particular show that the rejection of the back pressure mechanism

is unjustified We often see within a few hours the development of an enlarged liver and congestion of the peripheral veins in patients with atrial fibrillation or paroxysmal tachycardia with a rapid ventricular rate Rentention of water and increased blood volume could not play a part so soon Daily clinical experience reveals a marked pulmonary congestion but no increase of venous pressure or peripheral edema in patients with left ventricular failure or in patients with mitral stenosis and diminished cardiac output The pulmonary congestion in mitral stenosis diminishes when right ventricular failure supervenes On the other hand patients with pericardial adhesions or cor pulmonale with failure develop peripheral venous congestion and enlargement of the liver without any other signs of cardiac failure

Thus the back pressure mechanism does play a great part in the development of signs and symptoms of cardiac failure It is possible that it is the dominant mechanism in acute failure with the consequences of forward failure determining the picture in chronic heart failure (Dock)

The emphasis that has been laid upon the forward failure mechanism in recent years has aided in a better understanding of some aspects of heart failure Thus the influence of peripheral vasoconstriction — considered by Starling long ago — was completely neglected and only now has become better appreciated In a similar manner the increased amount of circulating blood in cardiac failure has been known for many years but its importance for the explanation of some features of cardiac failure is at present better understood

Cardiac catheterization enabled us to distinguish another type of cardiac failure high output failure It was found by investigators using methods available before cardiac catheterization for the determination of cardiac output that occasionally the cardiac output per minute was high despite the presence of failure In patients with emphysema and a lower oxygen saturation of the arterial blood hyperthyroidism with an increased oxygen consumption anemias with a disturbed oxygen transportation arteriovenous fistulas Paget s disease with an increased venous return and finally in beriberi disease with an abnormal tissue metabolism the circulation is markedly accelerated The cardiac output per minute at rest in anemia may amount to 10 liters in emphysema with marked oxygen undersaturation of the arterial blood it has been found to be 6 to 10 liters per minute If congestive failure develops the output falls but it is still higher than it is in patients with primary heart disease

Thus the mechanism in this group of patients does not differ from others When the heart fails the tissues are supplied with less blood than they need

MECHANISMS OF COMPENSATION

Compensation by Cardiac Dilatation

The importance of dilatation of the cardiac chambers for compensation becomes clear if we recall the changes following experimental valvular lesions An immediate result of aortic regurgitation is an increased flow of blood into the

left ventricle This structure receives a normal amount of blood from the left atrium plus the blood regurgitating from the aorta The increased content causes a stronger contraction and the output is larger by the volume of regurgitated or pendulum blood Despite the loss of some aortic blood by regurgitation during each diastole the minute volume remains normal If a marked aortic stenosis is created experimentally increased resistance prevents complete emptying for a few beats until the diastolic volume of the heart and the diastolic tension of its muscle fibers increase sufficiently to permit the output to reach a normal value The mechanism of compensation in hypertension operates in a similar way In myocardial lesions incomplete emptying of the heart is a factor in the dilatation

Hence dilatation of the cardiac chambers may be produced by any of these mechanisms i e increase of cardiac contents by regurgitation by augmented resistance to outflow (insufficient emptying) and finally by greater venous return The extent of cardiac dilatation is limited by the pericardium Dilatation permits the heart to maintain its output and within broad limits to compensate for abnormalities within the circulatory apparatus This dilatation is often minimal and cannot be recognized clinically or even by x ray examination

If the heart is unable to compensate for the lesion by means of the initial slight increase of filling and hypertrophy discussed above the amount of residual blood will increase and the dilatation is greater Thus a dilated heart is not necessarily a failing heart on the contrary dilatation is often a compensatory measure The left ventricle may dilate tremendously in aortic regurgitation and all signs and symptoms of heart failure may be missing However when the dilatation surpasses a certain limit cardiac output decreases

In normals it has been calculated that the residual blood within the cardiac chambers may amount to 50 ml rising as high as 2000 ml in cardiac failure

Compensation by an Increase of Rate

Another mechanism for rapidly increasing the output is a moderate acceleration of the heart rate While this may decrease diastolic filling of the heart somewhat the increased number of beats per minute may offset this and the net result may be a larger or even doubled minute output In many heart lesions acceleration that derives mainly from reflex action occurs very early

An increase of intraventricular pressure causes an immediate rise of pressure within the corresponding atrium for it is mainly the difference in pressure between the atrium and ventricle which causes ventricular filling Elevation of intra atrial pressure and the consequent dilatation of its wall and the walls of veins leading to the atrium cause a reflex tachycardia by means of the Bainbridge reflex The path of this reflex utilizes vagal and in part sympathetic fibers The effect of the reflex is diminished by atropine and disappears after extirpation of the stellate ganglion The exact location of the receptors is uncertain It is possible that no reflex is needed because when the right atrium is dilated the stretch

exerted on specialized fibers of the sinus node suffices to make the latter form faster impulses

Tachycardia appears very early in aortic insufficiency but in this instance a carotid sinus reflex is activated by the low mean blood pressure at the carotid sinus

While an acceleration of rate sinus tachycardia is often a useful measure of maintaining the minute volume in some conditions it may be harmful In mitral stenosis the tachycardia shortens diastole further hampering the filling of the left ventricle and adding to the pulmonary congestion As will be shown later a tachycardia increases oxygen requirements of the heart muscle and if the demand cannot be satisfied owing to disease of the coronary arteries myocardial nutrition suffers and the frequency of anginal attacks increases

Compensation by Hypertrophy

In cardiac hypertrophy the size of the myocardial fibers increases This increase in size always follows a primary dilatation since the fibers do not enlarge unless they increase in length and gain in tension Cardiac hypertrophy was fully developed in dogs within 80 days after an experimental lesion The border line is not sharp between physiologic cardiac hypertrophy of healthy athletes or people engaged in heavy physical work on the one hand and the hypertrophy consequent to increased filling or greater resistance on the other Hypertrophy enables the heart to perform the added task made necessary by greater filling However it also necessitates a much greater blood supply although there is no evidence to show that the number of capillaries increases in the hypertrophied heart Hence the size of the muscle fiber that can be adequately nourished by one capillary is limited There are reasons for believing that in some conditions e g stenosis of the aortic valve the hypertrophy reaches a point at which some layers of heart muscle are inadequately nourished and hypoxia of the myocardium results Furthermore the nuclei of the heart muscle cells do not grow and their number does not increase in hypertrophy Therefore limits are established for the growth of the protoplasm in hypertrophy

Whereas tachycardia and cardiac dilatation occur immediately if the need arises hypertrophy develops slowly when the added load for the heart has existed for some time Although hypertrophy does not appear without antecedent dilatation the latter may be too slight for demonstration by clinical methods This type of hypertrophy is called *concentric hypertrophy* a rather common occurrence in the left ventricle of patients with hypertension or in those with an aortic valve stenosis it is found in the right ventricle if a disease elevates the blood pressure in the lesser circuit When hypertrophy and more marked dilatation coexist the term *excentric hypertrophy* is used This form is encountered in the left ventricle in aortic regurgitation in connection with myocardial lesions or in coronary sclerosis If concentric hypertrophy changes to excentric hypertrophy one may assume that cardiac reserve is diminishing The evolution of this process may however require a considerable period of time

Raab stresses hormonal factors in the genesis of cardiac hypertrophy He refers to the large heart seen in acromegaly and the absence of hypertrophy after ligation of the aorta when an hypophysectomy had been done before

CHANGES IN THE AMOUNT OF CIRCULATING BLOOD AND OF TOTAL BLOOD VOLUME

The volume of circulating blood is reduced in a large number of cardiac patients By retaining a great quantity of blood the engorged liver and the markedly enlarged left atrium tend to prevent pulmonary congestion due to a stenotic mitral valve Accordingly patients with mitral valve disease and a large liver or with an enormous left atrium (aneurysm of the left auricle) often are remarkably free from pulmonary congestion and dyspnea This is understandable if one realizes that more than 2 000 ml of blood may be retained occasionally in the huge left atrium of mitral stenosis

If cardiac weakness or congestion lasts for a long time however the arterial oxygen deficit acts as a constant stimulus to the hemopoietic apparatus This stimulus is responsible for the increased production of red blood cells and an increase of the circulating and total blood volumes Many pathologists have directed attention to the large amount of blood found at necropsy in patients dying of congestive heart failure Such increased volume of circulating blood imposes a great burden on the heart and causes further slowing of the peripheral circulation As the peripheral blood depots become engorged the heart finds it increasingly difficult to adapt itself to the varying requirements

Wollheim distinguishes between minus decompensation (with diminished blood volume) as in myocardial infarction and plus decompensation (with increased blood volume and elevated venous pressure) in the usual type of cardiac failure

INCREASED UTILIZATION OF BLOOD

When contact between the blood and tissues is prolonged oxygen is utilized more completely and consequently the arteriovenous oxygen difference increases this may be a compensatory measure in congestive heart failure Actually the arteriovenous oxygen difference may double in heart failure and it may approximate the situation occurring in exertion In patients with congestive heart failure cardiac output cannot increase on exertion but there is an increase of the arteriovenous oxygen difference

RIGHT AND LEFT VENTRICULAR FAILURE

Mechanism

It is proper to distinguish between failure of the right and the left ventricle although some objections have been raised to the justification of this practice For example it has been stated that weakness of the left ventricle results in a decrease of its output therefore the return of blood to the right heart suffers since this is effected mainly by vis a tergo Accordingly the amount of blood

expelled by the right ventricle decreases to the same extent that the left ventricular output diminishes In this way stasis in the lesser circuit is avoided

Similarly in right ventricular failure less blood is propelled to the left heart so that its output is again reduced in proportion to the fall of right ventricular output Under these circumstances the return of blood to the right heart diminishes and stasis in the great veins and liver does not necessarily appear

While these presumptions are correct they are applicable only when it is assumed that the volume of circulating blood remains constant and the right heart invariably receives just as much blood as the left ventricle ejects It is this assumption which is incorrect The inflow of blood into the right heart undergoes continual variations for nervous as well as humoral regulatory mechanisms constantly control and adapt the amount of venous return to the heart in accordance with the momentary requirements of the organism A large amount of blood may be stored in depots (liver subcutaneous venous plexus splanchnic veins) if it is not needed and this depot blood may be suddenly mobilized and sent to the right heart if necessary When the inflow of blood increases suddenly the demands upon the heart are greater If the right or left ventricle has no reserve force available it is unequal to the burden causing backward stasis and congestion to develop The early consequence of heart failure is congestion upstream in the veins

In this way pulmonary congestion develops in left ventricular failure while hepatic congestion and engorgement of the systemic veins follow failure of the right ventricle If the entire heart is equally and simultaneously damaged so that both ventricles fail at the same time the clinical picture is the same as in ordinary right ventricular failure because congestion develops upstream of the heart with the result that hepatic enlargement and venous engorgement occur in the absence of pulmonary congestion This happens in cases of diffuse myocardial damage as in diphtheria and rheumatic fever Hepatic congestion is also seen in association with paroxysmal tachycardia or atrial fibrillation with a rapid ventricular rate With a tachycardia both ventricles contract rapidly and the inflow of blood into the right heart is impeded by the brevity of diastole

Relief Afforded by Right Ventricular Failure

In patients with pulmonary congestion and dyspnea the onset of right ventricular failure may afford speedy and remarkable relief If pulmonary congestion has become extreme and dyspnea and orthopnea have attained great intensity right ventricular failure with engorgement of the liver and systemic veins may change the situation completely Dyspnea and orthopnea diminish the vital capacity increases and x ray reveals less pulmonary congestion Naturally the development of peripheral edema and hepatomegaly now create new complaints but the dyspnea which harassed the patient day and night has lessened Since the patient soon becomes more or less accustomed to the discomfort evoked by the hepatic engorgement and since mercurial diuretics satisfactorily control the edema the grateful patient considers the new situation a vast improvement

This unloading of the lesser circuit fails to occur only when the state of the patient is precarious because of advanced pulmonary congestion Often the right heart is involved from the start and therefore pulmonary congestion of a high degree never develops Thus patients with rheumatic mitral stenosis who have a simultaneous tricuspid regurgitation need not within certain limits suffer from dyspnea or orthopnea If however the right heart works normally in a patient with mitral stenosis extreme pulmonary congestion may result since the barrier raised by the stenotic valve prevents blood from entering the left ventricle When it is recalled that a congested liver can retain approximately 1 500 ml of blood the relief of pulmonary congestion afforded by hepatic engorgement becomes comprehensible

Bernheim s Syndrome

In pronounced hypertrophy and dilatation of the left ventricle signs of right heart failure may appear without a preliminary period of pulmonary congestion Clinical observations by Bernheim suggested that in such cases the interventricular septum may bulge into the right ventricle and prevent a normal inflow of blood from the systemic veins The Bernheim syndrome is said to be especially encountered in patients with aortic stenosis and hypertension with marked cardiac hypertrophy A similar phenomenon has been seriously considered by physiologists On the basis of personal clinical and postmortem observations we accept the *possibility* of this mechanism although proof of its occurrence in patients with left ventricular hypertrophy is lacking The role this mechanism could play in diminishing back pressure in the lung and in relieving dyspnea is obvious

The only instances in which we consider this syndrome proved are cases of septal infarction with an aneurysmal bulge into the cavity of the right ventricle

Concluding Remarks

These observations show again how a multitude of factors interact in the production of different cardiac symptoms so that it is not advisable to infer the degree of heart failure from the severity of pulmonary symptoms

It should be clear that in practice right and left ventricular failure do not always appear in pure form nor do they have to appear in sequence for the clinical syndromes just discussed to emerge clearly Not rarely there is evidence of pulmonary as well as moderate congestion in the systemic circulation so that signs of right and left ventricular failure coexist Nevertheless an awareness of the rules outlined in this section may facilitate an understanding of both the variations in patients complaints and objective findings in the different stages of decompensation

DIAGNOSIS OF HEART FAILURE AND CONGESTION

To recognize the beginning of heart failure is difficult and often impossible Pulmonary congestion may be detected by careful interrogation designed to

elicit the subjective symptoms that accompany the condition Heart failure may be recognized by physical examination and by the evidence provided by roentgenography measurement of circulation time and venous pressure

One of the fundamental rules in the diagnosis of every case of heart failure is to endeavor to ascertain the reason for its occurrence Myocardial failure may be caused by excessive strain or by a primary disturbance of the myocardial fiber It is rare for the heart to fail gradually because of progressive dilatation Very often failure is precipitated by pulmonary embolism or paroxysmal atrial fibrillation in other instances an acute infection such as streptococcal tonsillitis or pharyngitis is responsible Among 300 patients with heart failure a respiratory tract infection was found in 167 in 150 it was the cause of heart failure (Flint) Overeating increase of weight mental and physical strain and progressive coronary sclerosis may be precipitating factors

If the precipitating cause is known its eradication can lead to a decided improvement of long duration This happens if atrial fibrillation with rapid ventricular rate is successfully treated with digitalis if foci of infection which damage the myocardium are removed if an anemia is abolished or if the patient recovers from a pulmonary embolism

According to Hegglin myocardial failure may be of hemodynamic origin that is it may result from fatigue and overexertion it may also be of energetic dynamic origin resulting from a primary disturbance of the heart muscle itself Energetic dynamic heart failure is a form of heart failure in which a shortening of the mechanical systole and a prolongation of the Q T interval are found (Hegglin) According to the author a heart in an abnormal metabolic state cannot maintain a systole of sufficient duration With a damaged myocardium the hemodynamically efficient systole is shortened (Wiggers) and this diminishes cardiac output If the blood supply to the myocardium via the coronary arteries is inadequate the heart becomes fatigued more quickly

Stimulation of receptors of the Jarisch Bezold reflex in the myocardium leads to an increased vagus tonus the heart is slowed and peripheral vessels dilate to protect the heart from overfilling

Clinical Diagnosis of Pulmonary Congestion

Clinical demonstration of pulmonary congestion may be so difficult that reliance must be placed upon the history of exertional dyspnea It should always be remembered however that dyspnea on effort occurs in other conditions e g obesity neurocirculatory asthenia or pulmonary diseases in the absence of congestive heart failure

As will be shown later cyanosis is not an unequivocal sign of pulmonary congestion and the determination of vital capacity yields little information The latter procedure has diagnostic value in slight pulmonary congestion only when comparative figures are available to indicate the status of the same patient prior to the onset of stasis but such information is rarely at hand Even elevation

of the diaphragm may diminish the vital capacity so that absolute values give little conclusive information Moreover accurate measurements are frequently difficult to obtain particularly in women

It should be emphasized that evidence of pulmonary congestion as well as dyspnea on exertion do not always prove that heart failure has occured In some conditions such as mitral stenosis pulmonary congestion is due to the valvular lesion and is present prior to heart failure

With more advanced stasis a cough develops and a brownish sputum is expectorated This sputum may contain macrophages containing hemosiderin i e heart failure cells or cells with a brownish stain If pulmonary congestion sets in abruptly moist crepitant rales are often audible over the bases of the lungs more commonly on the right side than on the left In chronic congestion the rales are often dry Even in the absence of other signs of heart failure the appearance of these rales in patients with conditions causing strain of the left ventricle such as hypertension myocardial or aortic lesions is an indication for digitalis therapy If digitalis is withheld congestion increases and pulmonary edema may occur without further warning This danger may also be averted by mercurial diuretics

The appearance of rales does not depend exclusively upon the severity of the pulmonary vascular engorgement thus in some patients with mitral lesions and pulmonary congestion of long duration relatively few rales and rhonchi are heard or only somewhat roughened expiration and intensified breath sounds are noted In long standing pulmonary congestion sclerosis of the pulmonary arterioles together with increased fibrosis and induration of the pulmonary tissue reduce the amount of fluid in the lung While large quantities of fluids exude from the lungs during necropsy of a patient who died from left ventricular failure caused by hypertension the lungs of patients with mitral stenosis and advanced pulmonary congestion of year long duration are dry Accordingly the absence of rales does not disprove the presence of pulmonary congestion

On the other hand some patients particularly elderly ones have moist rales over large areas of the lungs but principally in the basal region These rales which persist without modification for years despite intensive therapy are due to otherwise asymptomatic pleural adhesions obstructing the local lymphatic channels and causing transudation into the air passages Thus there is simulation of the auscultatory findings of pulmonary congestion

To distinguish between simple pulmonary congestion and infectious bronchitis is not always easy If the temperature is elevated and the protein content of the sputum increased bronchitis is the probable diagnosis However fever sometimes persisting for days is not uncommon in decompensation and is regarded as a consequence of stasis Formation of toxic substances due to hypoxia slowing of the circulation and therefore local disturbances in the thermal regulatory mechanisms in the periphery and lessened heat dispersal are responsible for a moderate rise of temperature If the temperature surpasses one degree Celsius above normal a complication such as pulmonary infarction probably exists

When emphysema is present in combination with fever and rales the findings are sometimes interpreted to be evidence of a primary pulmonary disorder and the underlying cardiac pathology is overlooked This is a common occurrence in those *cases in which no abnormal auscultatory cardiac findings are present*

In pulmonary congestion the second pulmonic sound becomes accentuated but it will be shown later that this sign has only limited clinical value

With progressive failure of the left ventricle dilatation of the left atrium is *an early development Hypertrophy and moderate dilatation of the right ven* tricle especially of the outflow tract gradually develop and the heart becomes mitralized on percussion

This discussion should make clear that a roentgenologic examination is often indispensable for the demonstration of pulmonary stasis especially in its initial state

Roentgenologic Diagnosis of Pulmonary Congestion

A history of increasing exertional dyspnea aids considerably in the early diagnosis of pulmonary congestion even when physical diagnostic methods yield little pathognomonic evidence Roentgenoscopy and roentgenography are invaluable for providing reliable objective data

Pulmonary congestion causes engorgement of the blood vessels and therefore creates large hilar shadows with increased pulsation and accentuated pulmonary markings It has been estimated that congested lungs may hold twice as much blood as normal ones without increase of pulmonary arterial pressure Congestion of the perivascular and peribronchial lymph vessels contributes decidedly to the increase of pulmonary markings whereas enlargement of lymph glands accentuates the hilar shadows Later cloudiness of the lung fields increases and these changes may be general or circumscribed This cloudiness and mottling is due to transudation into the alveoli distention of the pulmonary capillaries and particularly to the dilatation of the lymphatics Since the lymphatics are more numerous and larger where the large bronchi and blood vessels bifurcate cloudy areas with ill defined borders often appear Formerly these shadows were confused with those of intrinsic diseases of the pulmonary parenchyma (Zdansky)

The lungs become less transparent and the definition of the heart and vessels less distinct *In rare cases of pulmonary congestion the lungs display innumerable* small shadows scattered diffusely throughout and give the impression that miliary tuberculosis may be present Pulmonary congestion causes hemosiderosis and *fine granulation resembling pneumoconiosis miliary tuberculosis or Boeck s* sarcoid This impression is also created by small bronchi seen end on and filled with heart failure cells

In chronic congestion increased markings and abnormal shadows in the lungs are also due to progressive pulmonary fibrosis (resulting from hyperplastic con nective tissue and from reactive and reparative processes following intrapulmonary *hemorrhages) and to sclerosis of the pulmonary arteries Since intrapulmonic*

transudates form predominantly in the poorly ventilated areas local atelectasis may result

A new x ray sign of pulmonary congestion has been described recently by Kerley Two to 15 horizontal lines up to 2 mm in thickness and 0 5 to 1 cm



FIG 17 Kerley lines in the right lung field of a 32 year old patient with rheumatic mitral stenosis

apart and 5 to 15 mm in length are seen in the costophrenic angle perpendicularly to the lateral chest wall They are most common in mitral stenosis but they also appear in pulmonary congestion of other etiology They are called

septal lines since the precipitation of hemosiderin and edema in the interlobular septa is responsible Short found these lines in 25 of 33 patients with severe mitral stenosis

Figure 17 shows Kerley lines in a patient with mitral stenosis and a large left atrium They must be differentiated from blurred vessels which usually communicate with each other In Figure 17 one of the horizontal lines stops short of the vascular shadow while the other extends beyond it

Pleural adhesions as well as local pulmonary indurations the sequelae of old infarctions and hemorrhages account for the irregular distribution of congested areas

When pulmonary congestion develops rather abruptly the lung fields become less clear and clouding appears but there are no hilar changes so characteristic of chronic passive congestion of the lungs

CYANOSIS

An increased amount of reduced hemoglobin in the arterial (capillary) blood is responsible for cyanosis the bluish color of the skin observed in connection with cardiac lesions Cyanosis appears as soon as reduced hemoglobin amounts to 5 Gm per 100 ml of arterial blood Since 1 Gm of hemoglobin unites with about 1 34 ml of oxygen 6 7 per cent oxygen unsaturation will be present when cyanosis appears (Lundsgaard and van Slyke) the normal figure for oxygen unsaturation is approximately 3 5 per cent While the occurrence of cyanosis depends entirely upon the amount of reduced hemoglobin its depth as well as its early discovery are influenced by the thickness of the skin pigmentation and the number of capillaries Cyanosis appears earliest where the skin is thin i e in the lips fingertips and nail beds

If the patient is severely anemic cyanosis never occurs since 5 Gm of reduced hemoglobin per 100 ml of blood the necessary amount cannot be present On the contrary patients with polycythemia and an otherwise normal circulation may display cyanosis constantly because the percentage of oxygen unsaturation per 100 ml of blood easily reaches the critical level

In cardiac patients cyanosis or an increased amount of reduced hemoglobin in the arterial blood may originate in four different ways

(1) In congenital heart lesions the arterial and venous systems often communicate abnormally (malformations of the septa riding aorta transposition of the aortic and pulmonic orifices) and venous blood is shunted into the arterial system The presence of increased amounts of reduced hemoglobin in the arteries of these patients requires no discussion although it should be noted that at least one third of the venous blood must be short circuited for cyanosis to appear

A large percentage of congenital heart lesions however belong to the so called acyanotic group despite the existence of an abnormal communication between the arterial and venous systems as a result of a left to right shunt Normally pressure in the left atrium left ventricle and aorta is higher than in the

right atrium right ventricle and pulmonary artery Therefore arterial blood flows into the venous system without venous blood entering the arterial so that cyanosis is absent Not infrequently however activities like coughing or crying spells or complications like pulmonary or mitral stenosis elevate the pressure in the right heart sufficiently to force venous blood into the arterial side in amounts adequate for the production of cyanosis Of course in children crying spells may cause cyanosis under normal conditions owing to the prevention of inflow of blood into the chest during pressing and straining

(2) Slow peripheral circulation the result of dilated peripheral vessels or congestion and increased venous pressure permits prolonged contact between the blood and tissues thereby increasing oxygen utilization In this way the amount of reduced hemoglobin in the capillary blood rises (stagnant anoxemia) The cyanosis found in patients with pericardial adhesions and inflow stasis or some cases of right heart failure belongs in this group

This form of cyanosis also occurs in the absence of heart disease Not rarely patients are referred for a cardiac examination because they exhibit a striking cyanosis of the lips or fingers this creates the suspicion that organic heart disease exists In actuality nothing more than a slow peripheral circulation resulting from dilatation of the peripheral vessels is present The causative factor varies In many cases there is a constitutional widening of the peripheral vessels in some parts of the body in others vascular dilatation appears after prolonged exposure to cold weather or by virtue of some disturbance of unknown etiology (acrocyanosis) This type of cyanosis is easily recognized by the cyanotic parts — lips fingers tip of the nose or lobes of the ears — feeling cold to the touch Owing to the retarded circulation less warm blood than normal enters these tissues per minute consequently this kind of cyanosis is called cold cyanosis and can be distinguished from other varieties by palpation

(3) Cyanosis conceivably may occur when oxygen utilization in the tissues is increased for other reasons Thus an increase of the arteriovenous oxygen difference in cardiac patients is an important cause of cyanosis

(4) The fourth and most important form of cyanosis in circulatory disorders of which two subvarieties are distinguished depends upon abnormal oxygenation of the blood in the lungs

(a) PULMONARY STASIS If the pulmonary circulation is slow in the absence of any other disturbance oxygenation of the blood should be excellent for the corpuscles have a better opportunity for gas exchange with alveolar air Widening of the capillary bed however prevents some of the red blood cells from coming in contact with the alveolar wall Furthermore congestion alters the pulmonary epithelium or capillary endothelium and prevents the normal exchange of oxygen Carbon dioxide due to its greater permeability is not retained The interaction of all these factors is the reason that the depth of cyanosis does not strictly parallel the degree of congestion Indeed decided pulmonary congestion may be unaccompanied by cyanosis

Like the dyspnea of pulmonary congestion cyanosis may diminish if super vening right heart failure and hepatic enlargement reduce pulmonary congestion Rapid failure of the right heart often diminishes rather than accentuates a pre viously existing cyanosis Such patients may become quite pale because of the large amount of blood that is retained in the liver Marked cyanosis is not a regular sign of right heart failure If such patients show a deep cyanosis an underlying pulmonary disease or severe venous congestion is usually responsible

In pneumonia and more rarely in pulmonary infarction cyanosis may appear when large amounts of blood are shunted from the pulmonary arteries to the pulmonary veins without undergoing arterialization

(b) PULMONARY SCLEROSIS ESSENTIAL PULMONARY HYPERTENSION Primary sclerosis of the larger arteries in the lesser circuit is extremely common Athero sclerosis of these vessels is no rarer than in the systemic circulation Approximate ly one half of all individuals beyond the age of fifty years exhibit this lesion and senile pulmonary sclerosis is almost invariable in patients over seventy years of age This variety is asymptomatic

Another primary form of pulmonary sclerosis the Averza or Averza Arrillaga syndrome involves the smaller peripheral arteries Its pathogenesis is not clear Syphilis formerly considered provocative does not play any role Bronchopneu monia has been assumed without justification to be the initial lesion Some form of primary arterial involvement may contribute to the development of this disease Such cases may have been instances of essential pulmonary hypertension in which an unknown mechanism increases pressure in the lesser circuit It may be assumed that we are not dealing with a disease entity and that different conditions causing pulmonary arterial hypertension are responsible

Patients with pulmonary hypertension display a deep blue cyanosis (cardiacos negros) and trivial dyspnea This disparity between the depth of cyanosis and the mildness of the dyspnea is remarkable Headache vertigo somnolence cough hemoptysis and anginal pain are typical symptoms A polycythemia which may reach ten million red blood cells per cubic millimeter is common and contributes to the cyanosis Physical examination discloses evidence of right ventricular hypertrophy *The conus of the pulmonary artery and its branches are prominent* and the second pulmonic sound is accentuated A systolic murmur is often audible over the pulmonic orifice and moderate pulmonary emphysema may be found Clubbing of the fingers is common Congestive heart failure with hepatomegaly edema and ascites appear early Ordinarily the disease runs a rapid course after the appearance of symptoms Frequent phlebotomy with the removal of relatively small amounts of blood (200 ml) may afford some symptomatic relief

Sclerosis of small pulmonary arteries due to stasis (secondary sclerosis) is a common event when the pulmonary vessels are engorged for a long time The small precapillary arteries are involved in the same way the peripheral arterioles are affected in systemic hypertension This sclerosis is common in rheumatic mitral stenosis It also develops regularly although in varying degree in other conditions associated with increased pressure in the lesser circuit these conditions

are exemplified by congenital heart lesions emphysema kyphoscoliosis fibrotic pulmonary tuberculosis and extensive pleural adhesions

The etiologic significance of elevated pressure in the lesser circuit for the development of pulmonary atherosclerosis is emphasized by the readiness with which this lesion develops in childhood when transposition of the large vessels patent ductus arteriosus or a defect in the interventricular septum create an abnormally high pressure in the lesser circuit

HYPOSTATIC CONGESTION AND PNEUMONIA

In debilitated patients who do not change their position for a long time and who do have congestive heart failure hypostatic congestion develops in the dependent parts of the lungs Sudden infiltration and pneumonia may develop in these areas Hypostatic pneumonia is often diagnosed when pulmonary embolism with infarction exists

INCREASED BASAL METABOLISM

An increased basal metabolic rate so often found in patients with cardiac failure is due to the dyspnea the increased temperature intake of more oxygen because of tissue anoxia excitement and other unknown factors

MENTAL DISTURBANCES

Insomnia a mild depression or greater irritability are common in heart failure particularly in the presence of Cheyne Stokes breathing Delirium mental confusion hallucinations may occur Cerebral edema is in part responsible

FATIGUE

Marked fatigue is a common symptom in cardiac patients and particularly among those with arteriosclerosis Often it is the only complaint Sometimes this symptom stems from a diminished intake of thiamine in which case it is easily treated In patients who have been on a salt free diet for a long time the fatigue is the result of sodium chloride deprivation Sometimes it is a symptom of an anxiety neurosis A diminished content of potassium in the skeletal muscle has been held responsible In many cases digitalis therapy may help and it is probable that tissue anoxia due to the lowered cardiac output is an etiologic factor In most cases however no reason for the fatigue is found and the symptom often vanishes after having been present for months with no change in the objective findings

HEPATIC ENLARGEMENT

Engorgement of the liver is properly regarded as the earliest sign of right heart failure The liver is located directly upstream from the right heart and is separated from the inferior vena cava and right atrium only by the wide valveless

hepatic veins The left lobe of the liver seems to enlarge first in cardiac patients probably owing to the anatomic arrangement of the hepatic veins and their branches For this reason patients with hepatic engorgement rarely complain of pain in the right side of the abdomen Instead relief from stomach pain is sought since the distress is felt in the epigastrium Some time may elapse before it is realized that swelling of the liver and not a gastric disorder is responsible for the pain

At first this pain may be experienced only after meals which tends to confirm the patient s opinion that it is of a gastric origin Sometimes it occurs only on exertion (Boyer and White)

Not every congested liver causes pain or is tender on palpation Congestion frequently enlarges the liver so much that the upper portion of the right abdomen bulges although the patient reports nothing more than epigastric fullness no pain is elicited by pressure or palpation In such cases the congestion is slow in onset or of long duration The more acutely right heart failure develops the more marked is hepatic pain Therefore both the presence or absence of pain and tenderness on pressure in the hepatic area are valuable means of appraising the speed with which right heart failure develops or its duration If an already enlarged liver again becomes sensitive on pressure progressive right heart failure is present even if no other signs support this conclusion For the reasons mentioned the gradual development of hepatomegaly in pericardial adhesions precludes sensitivity of the liver On the other hand the hepatic engorgement resulting from paroxysmal tachycardia (paroxysmal fibrillation) or right heart failure from pulmonary embolism develops acutely producing pain and tenderness of the liver on palpation

The pain from an acute hepatic engorgement is not felt exclusively over the liver it may radiate to the right shoulder and be mistaken for arthralgia

Meteorism and nausea appear in many cases of hepatic congestion an increased excretion of urobilinogen and urobilin are regular findings The stasis gastritis aggravates the symptoms The distention of the intestines increases the abdominal pressure and decreases the venous backflow and thus may enhance edema formation

Vomiting is a common manifestation of acute hepatic engorgement and presumably is the result of peritoneal irritation The ominous vomiting that occurs in patients with diphtheria and acute heart failure as well as that appearing in patients with paroxysmal tachycardia is a well known phenomenon Hepatic enlargement and vomiting is not infrequent in patients who receive digitalis in small amounts Indeed the physician often ascribes the vomiting to this drug and discontinues it but the fact is that the vomiting ceases quickly if increased amounts of digitalis are administered since this symptom results from progressive heart failure

Enlargement of the liver may be seen in right heart failure at a time when the venous pressure is still not yet increased this is explained by the fact that the hepatic veins flow into the inferior vena cava at an angle of almost 90 degrees

thus producing an early congestion that would not be produced were the angle less than 90°

The retention of approximately 1500 ml of blood in a congested liver and the consequent withdrawal of this amount from the circulation may cause pulmonary congestion to diminish and dyspnea as well as cyanosis to disappear

Histologically the congested liver shows a typical widening of the central vein with necrosis of the central cells This seems to be caused by hypoxia because this portion of the liver lobule receives less oxygen

Heart failure with chronic hepatic congestion is claimed to be responsible for attacks of hypoglycemia with sudden weakness sweating palpitation and nervousness Psychoses convulsions and coma may also appear As the result of congestion a nutmeg liver may develop and the amount of fibrotic tissue may gradually increase in the central part of the lobule This increase was found in one third of 286 cases of chronic passive congestion of the liver Congestive cirrhosis with splenomegaly gradually develops In recent years this has become a more common finding since mercurial diuretics prolong the life of these patients for years formerly death occurred before congestive cirrhosis of the liver could develop

Liver function in patients with congestive heart failure may be disturbed Direct and indirect bilirubin in the serum is raised in heart failure corresponding to the degree of liver congestion Different tests of hepatic function show abnormalities such as the tendency to lower albumin and greater globulin levels in the serum

Congestion of the intestinal tract in patients with engorgement of the liver leads to meteorism eructations and the sensation of fullness The meteorism is due to diminished reabsorption of gases caused by venous congestion (Schoen)

JAUNDICE

The skin and sclera may become slightly yellow (subicteric tint) in patients with congestive heart failure and evident hepatic congestion Jaundice appears because the pulmonary congestion is associated with destruction of many red blood cells while the liver damage in right heart failure the result of hypoxia impairs its excretory function If jaundice becomes pronounced pulmonary infarction should always be suspected

Large amounts of urobilin and urobilinogen and even (rarely) bilirubin may be excreted in the urine The van den Bergh reaction in the blood serum is usually delayed and indirect as in hemolytic jaundice of other origin but a direct reaction may be obtained with greater liver damage

If the patient has edema jaundice may be absent from the edematous areas

EDEMA

The formation of edema in most cardiac patients is the result of multiple rather than single factors While a marked alteration of one of the mechanisms about to be described may be provocative usually a number of abnormal con

ditions interact to produce edema (In this respect one is reminded of the mechanism of dyspnea)

The movement of water through the capillary wall into the tissues depends mainly upon the intravascular (hydrostatic) pressure the centrifugal force which drives water into the tissue and the colloidosmotic (oncotic) pressure of the plasma proteins as the major opposing force which tends to retain water within the vessels Both of these factors in turn are opposed by the hydrostatic and colloidosmotic pressure of the tissue fluids

Normally the forces are so balanced that the quantity of fluid pressed through the capillary membrane into the tissue equals the amount removed by the lymphatics or discharged back into the capillaries Three factors were formerly held responsible

Increased Venous Pressure Under normal conditions the hydrostatic pressure in the arterial section of the capillaries is higher than all opposing forces and therefore plasma passes into the tissue spaces Since this hydrostatic pressure is lower in the venous limb of the capillary fluid passes from the tissues to the capillary in this area This mechanism is altered if venous pressure is increased A high venous pressure also impedes the flow of lymph because the entrance of lymph into the large veins in the upper thorax will be retarded as well Mechanical compression of veins causes edema The amount of edema however does not parallel the height of venous pressure Even ligation of the inferior vena cava frequently does not result in the formation of edema

While other factors are of greater importance venous engorgement has importance in the formation of edema This mechanism explains why edema of cardiac patients is dependent and collects at points where venous pressure is particularly high It also makes clear why patients with pericardial adhesions and inflow stasis due to compression of the superior vena cava have facial edema only when in the supine position Their edema disappears in the erect posture because of the consequent lowering of pressure in the tributaries of the superior vena cava

Increased Permeability of the Capillary Endothelium If the circulation is disturbed and the oxygen supply to the tissues diminished the capillaries may become more permeable to water and crystalloids The development of tissue anoxia is enhanced by the increased oxygen requirements of the tissues (increased basal metabolic rate) in decompensated cardiac patients However the low protein content of the edema fluid and the absence of hemoconcentration in acute heart failure with edema formation show that this factor is not solely responsible With severe anoxia in patients with pulmonary diseases and congenital heart lesions edema is often absent

Hypoproteinemia Cardiac patients often have a relatively low level of serum proteins as the result of several factors such as the great loss of albumin in the urine when renal congestion is present Hypoproteinemia may also stem from malnutrition Great loss of proteins also occurs in conjunction with edema and transudates This loss of protein may be great if hydrothorax and ascites develop

and their evacuation by paracentesis is necessary If the critical level of plasma proteins is reached (5 5 Gm of plasma proteins with 2 5 Gm of plasma albumin per 100 ml of plasma) edema appears occasionally The oncotic pressure of the serum is diminished in cardiac patients even before edema forms The serum *protein level is said to fall in right but not in left heart failure (Kagan)*

Other Causes The pathogenesis of diffuse and circumscribed edemas which appear in women suffering from climacteric disturbances or during the menstrual period is obscure It is most probably connected with the retention of sodium caused by the sex hormones Injection of crystalline preparations of estrone progesterone and pregnandiol causes water sodium and chloride retention in normal dogs (Thorn et al) Similar retention is observed premenstrually in humans these substances are excreted in increased amounts at the beginning of menstruation Such patients suffer from headaches fatigue vertigo and even mental aberration

New Concepts of the Mechanism of Edema

In acute hemorrhage and in certain types of shock a widespread vasoconstriction occurs this has been claimed to be a useful phenomenon (by addicts of teleologic reasoning) because it diverts blood from less vital organs to more important ones — the heart brain and kidney The arteries of these organs were said not to participate in the general vasoconstriction In recent years it has become increasingly clear that this concept is fallacious Attacks of sudden blindness that have been observed after acute hemorrhage indicate participation of the retinal arteries in the general vasospasm We were able to show that marked electrocardiographic changes appear temporarily in a majority of patients with acute hemorrhage thus demonstrating the participation of the coronary arteries Experimental investigations and the finding of azotemia following a profuse hemorrhage show that a reduction of renal circulation also exists in these patients

Patients with cardiac failure respond in a similar manner as those with an acute hemorrhage Here also — as pointed out earlier — general vasoconstriction takes place as a consequence of the diminution of cardiac output However while in other organs the diminished blood supply parallels and corresponds to the diminution of cardiac output renal blood flow is reduced out of all proportion If the cardiac output is reduced to one half its normal value renal blood flow is reduced to 20—30 per cent of normal which in turn causes a reduction of the filtration rate in the kidney to 50—75 per cent of normal This is said to be accomplished by the constriction of the efferent and according to some investigators the afferent glomerular arterioles The mechanism of the event is still not clear Tubular function seems to be unchanged while owing to the presence of diminished filtration rate with normal reabsorption in the tubuli more sodium and consequently more water is retained According to others (Davies and Kilpatrick Sinclair Smith and others) the tubular absorption of sodium is actually increased

Thus a response which is useful in acute hemorrhage — to a degree — for the preservation of the species by conserving electrolytes and fluids and by lessen

ing their excretion through the kidneys leads in heart failure to the formation of edema

According to Starling s rules of equilibrium (see p 83) cardiac failure leads to increased venous and capillary pressure This causes the transudation of fluid (edema) The consequent reduction of plasma volume causes retention of salt and water According to the new conception cardiac failure causes via the renal mechanisms just mentioned retention of salt and water the plasma volume expands the venous and capillary pressures rise and transudation into the tissues takes place

The new conception lacks universal approval The necessity of accepting Starling s rules of osmotic and hydrostatic equilibrium is stressed (Peters) and so is the important part which the increase of venous pressure plays in edema formation According to some authors (Miller) the initial phenomenon is retention of water sodium being retained secondarily For many years the discussion has been going on whether venous pressure must rise before edema appears (Jouve and Vague) The experiments of Starr in which it was demonstrated that in resting dogs very severe damage of the right ventricle by burning need not cause a conspicuous increase of venous pressure do not prove too much since increased venous pressure would in all probability have been found had the dogs been forced to work In patients with severe acute myocardial infarction following coronary occlusion we see no congestion unless heavier meals or physical exertion increase the amount of circulating blood The venous bed is wide and can be expanded the venous pressure need not rise immediately therefore when right ventricular failure appears

The participation and the degree of action of hormones from the adrenal cortex and hypophysis in edema formation has not been elucidated It may be assumed that these hormones control the excretion of sodium and water (Raab Singer and Wener Bornstein Hanenson et al) Raab elicited the clinical picture of congestive heart failure by overdosage with adrenocorticotropic hormone

The part played by the antidiuretic hormone of the hypophysis and the sodium retaining corticoid aldosterone is under active investigation The excretion of aldosterone in the urine is markedly increased in heart patients with cardiac failure and edema A temporary increase is also seen in patients with acute myocardial infarction (Wolff)

An inadequate cardiac output causes a discharge of adrenocortical hormone and a discharge of posterior pituitary hormone The hormonal action on tubular reabsorption of salt and water may thus play a paramount part in the formation of edema in cardiac failure (see Hamilton)

While the finer mechanism of the diminution of the renal excretion of sodium and water is unknown there is no doubt that renal blood flow is diminished in cardiac failure These investigations were significant since physicians were again led to realize the importance of sodium in the genesis of edema a point stressed by Widal and others more than 50 years ago

The early recognition of water retention is very difficult. When edema becomes visible and when pitting appears a considerable amount of water has already been retained in the body: about 5 to 6 kilograms are retained before pitting is demonstrable. Edema can be detected by palpation if the size of the limb has increased 8 to 10 per cent. Accordingly, an accurate record of the patient's weight is the most reliable simple method of following water balance when retention is suspected or discovery of recurring edema is important. Several tests have been advocated for early diagnosis of water retention but they are not reliable and for the most part have been abandoned.

In elderly as well as in obese patients edema often appears in the absence of demonstrable cardiac damage. It is a common event during periods of continued warm weather. Individuals who stand quietly without moving their legs may develop ankle edema. Edema appearing in only one lower extremity is not of cardiac origin; superficial or deep varices or deformities of the foot (fallen arches and the like) are more likely causes.

If the skin becomes wrinkled over an edematous area the edema is receding provided no alteration of position has occurred.

The edema may be hard or soft. Hard edema is usually chronic and exhibits changes in the connective tissue. Occasionally this type — which may be painful — is found in the abdominal wall but rarely above the level of the umbilicus. Thrombosis of the deep veins of the abdominal wall apparently is the major etiologic factor.

Sometimes bilateral edema of the hands and arms appears in very advanced heart failure when venous pressure is markedly raised. Unilateral edema of an arm may develop in this stage if the patient has increased local venous pressure brought about by lying on the affected side. Thrombosis of the jugular vein causes unilateral edema of the arm, the face and the breast on the corresponding side. If the superficial vessels of the neck become thrombosed the jugular veins may be palpable as hard cords.

Massive edema and necrosis of the toes and occasionally also of the ear and tip of the nose have been observed in connection with ball thrombi of the left atrium (see later).

When the patient is confined to bed the examination should include inspection and palpation of the sacral region, for cardiac edema is a gravity edema and collects in the most dependent part.

There is no parallelism between the severity of the decompensation and the degree of edema. This must be anticipated since the edema is usually the result of an interplay between several mechanisms.

HYDROTHORAX

One of the earliest signs of decompensation that often antedates all other evidence of cardiac failure by months is hydrothorax.

In most cardiac patients hydrothorax is more prominent on the right side. It may be absent on the left side even when a massive effusion exists on the right.

It has been maintained recently that a right sided effusion appears most commonly in patients with mitral lesions in combined left and right heart failure and in atrial fibrillation whereas a left sided effusion is more common in patients with left ventricular failure An enlarged left ventricle is alleged by compression to impede the circulation in the left pulmonary veins while a dilated right atrium hampers the return from the right pulmonary veins Exceptions to these rules are by no means uncommon and in our opinion right sided effusion is the rule, irrespective of the etiology of the heart failure

Very often the appearance of a right hydrothorax follows infarction in the middle or lower lobe of the right lung Infarction in the left lung may cause a left sided effusion If the right pleural cavity is obliterated by adhesions and the conditions prevail in which a hydrothorax develops the effusion can form only on the left side Right pleural adhesions are common in cardiac patients with chronic failure due to repeated pulmonary infarction Left sided effusions sometimes develop after coronary thrombosis

Many hypotheses have been devised to explain the high incidence of effusions into the right pleural cavity Some of these theories assume that an enlarged right atrium compresses the azygos vein or that differences of intrathoracic pressure play a role It has al o been stated that the average venous pulmonic pressure is higher in the right lung especially with the patient in the preferred right recumbent posture The pulmonary venous blood from the right lung must be lifted more than that from the left lung to reach the left atrium (Dock) The volume of the right lung seems to be 10 per cent larger than that of the left This makes the surface exuding fluid larger Convincing proof to support either explanation however is lacking

Hydrothorax may develop in right or left heart failure The veins of the parietal pleura drain for the most part into the azygos system whereas the veins of the visceral pleura send their blood mainly into the pulmonary veins Therefore increase of pressure in either atrium may lead to edema Pulmonary engorgement seems to be the chief factor in the development of hydrothorax

Bilateral hydrothorax is an early and rather regular phenomenon in acute hemorrhagic nephritis and is indicative of the general capillary damage in this condition

When hydrothorax persists for some time (it may last for years) its protein content may be relatively high so that the differential diagnosis between an exudate and transudate is impossible by the usual laboratory tests

X ray permits an earlier diagnosis of hydrothorax than does physical examination since a considerable amount of fluid at least 500 ml must collect in the pleural cavity before physical examination will disclose it Moreover x ray examination is invaluable for the diagnosis of interlobar effusions which are not uncommon on the right side when adhesions have been created by previous pulmonary infarctions It should be emphasized however that the fibrotic tissue of pleural adhesions may become so edematous that a differential diagnosis by x ray between edematous adhesions and a free hydrothorax is difficult This

difficulty becomes more comprehensible when one recalls that free pleural effusions usually develop first along the visceral pleura and therefore cause x ray findings which resemble pleural adhesions

If a massive hydrothorax is added to the pulmonary congestion and to the enlarged heart the vital capacity is markedly reduced for mechanical reasons the resultant cyanosis and dyspnea may be very pronounced

ASCITES

If ascites dominates the clinical picture severe passive congestion in the portal circulation should be suspected Under these circumstances two conditions deserve serious consideration First tricuspid insufficiency may be present usually this is easily recognized by the expansile pulsation of the liver and the positive venous pulse in the neck Second the inferior vena cava or hepatic veins may be compressed by adhesions at the base of the right lung or by pericardial adhesions In many patients the thin walled hepatic veins empty into the inferior vena cava in part or entirely above the diaphragm Consequently they are readily compressed by a pericardial effusion or adhesions in this region Ascites may however also appear in conditions other than tricuspid and pericardial lesions e g occasionally in syphilitic aortic regurgitation

It is of practical importance to note that effusions in the pleural and peritoneal cavities are continuously absorbed and reformed It has been estimated that 40 to 80 per cent of the ascitic fluid enters and leaves the abdominal cavity per hour[1] The appearance of ascites is based upon the fact that the outpouring of lymph into the peritoneal cavity continuously exceeds normal In ascites reabsorption is affected by the venous congestion This continuous circulation of the effusion in the pleural and abdominal cavities explains the diuretic effect that follows the injection of mercurial diuretics into ascitic fluid or into a hydrothorax

RENAL CONGESTION

Congestion of the kidneys produces changes in the urine which are often characteristic The urine is concentrated and the specific gravity may be as high as 1 035 If allowed to stand a few hours after it is voided the urine is dark red in color because of the presence of large amounts of urobilin Albuminuria is usually present and may be pronounced The number of granular casts likewise increases There may be 10 times as many red blood cells as in the urine of a healthy individual

The discovery of a marked albuminuria in conjunction with casts and increased number of red blood cells in the urinary sediment may create the wrong impression of a primary renal lesion especially when the blood pressure is high The great increase in the specific gravity of the urine and its high content of urobilin and urobilinogen speak in favor of renal congestion

Many tests have been introduced for the evaluation of renal function The simplest and best is one of the modifications of Volhard s dilution and concen

tration test An amount of 1000—1500 ml of water is taken and one observes whether this fluid is excreted within four hours During the day the patient is not allowed any fluid and the specific gravity of the urine should gradually rise to values above 1 025 in the healthy It should be stressed that this test is applicable for the determination of renal function only when there is no evidence of congestive heart failure If the latter is present or imminent retention of the ingested water is marked and abnormal values of the urinary specific gravity are obtained

The blood nonprotein nitrogen and urea may be abnormally high in congestive heart failure or following myocardial infarction The values return to normal soon after improvement begins In such cases some intrinsic renal lesion like atherosclerosis or arteriolosclerosis is often present in addition to congestive heart failure While the renal lesion does not suffice to create any disturbance it causes azotemia as soon as some circulatory disturbance is superimposed Precipitous fall of blood pressure in myocardial infarction leads to azotemia by the same mechanism as in acute blood loss that is narrowing of the arterial tree particularly in the kidneys Nonprotein nitrogen may also increase as the result of too energetic treatment with mercurial diuretics in an attempt to relieve edema

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Chapter 6

The Circulation Time

THE VELOCITY OF BLOOD FLOW is ascertained by measuring the so called circulation time In clinical medicine the circulation time is found by introducing some substance into the circulation and determining the time required for its arrival in sufficient quantities at another point to produce either an objective response or a response determined by other methods

Substances Used Many substances have been suggested among which may be mentioned ether lobeline sodium cyanide aminophyllin fluorescein saccharine histamine calcium chloride radium magnesium sulphate sodium dehydrocholate labeled erythrocytes calcium gluconate sodium succinate methylene blue and congo red Some of these substances possess the advantage of giving responses that are amenable to objective observation

Methods and Normal Values Ordinarily the circulation time is measured from the moment of injection to the appearance of the substance in the skin tongue carotid sinus an artery of the opposite arm etc Even when the test is performed with great care and with the patient under basal conditions the values for normal circulation vary The normal arm to skin time varies from 9 to 20 seconds according to the method used The injected substance naturally appears earlier in the arm than in the leg (approximately half the time)

The arm to lung circulation time is measured with the aid of ether Ether (0 25—0 33 ml) and saline (0 5) ml are injected intravenously and a cough deep breath or the smell of ether on the breath is considered the subjective and objective endpoint Other substances have also been used — paraldehyde for example also elicits a cough reflex Arm lung times of four to eight seconds are considered normal

With a combination of these methods i e by measuring the arm to lung and the arm to tongue time it is possible to calculate the lung to tongue time or the velocity from the lung to some part of the systemic circulation

The circulation time is greater when the blood volume is increased and shorter when the cardiac output rises Cardiac output is increased with higher room temperature It may rise 40 per cent after a meal and 100 per cent during anxiety

Of great importance is the discovery by Nylin and his collaborators that in dilated hearts the circulation time is prolonged because the injected substance is mixed with the enormously increased residual blood in the dilated cardiac chambers Under normal conditions the heart has a capacity of 400 ml The heart

of a patient with aortic insufficiency may have a capacity of 3000 ml and the amount of residual blood may exceed 2000 ml Therefore in patients with enlarged heart an increased circulation time does not necessarily indicate a slower blood flow

To obtain a reliable test the physician should have the patient rest comfortably for at least 20 minutes before the test is taken

Interpretation Since the speed of the blood flow in the arterial part of the circulation (pulmonary artery and its tree aorta and its vascular branches) is not remarkably altered even in advanced heart failure prolongation of the arm to lung circulation indicates a delay in the flow in the systemic veins in right heart failure In heart failure the figures for arm to skin and arm to lung circulation may be trebled With a normal arm to lung circulation time prolongation of the arm to tongue circulation time indicates a delay in the pulmonary veins caused by left heart failure

The circulation time is decreased in beriberi anemia fever and hyperthyroidism It is also shortened in arteriovenous fistulas and in congenital heart disease with a right to left shunt It is increased in myxedema

The values of circulation time do not parallel the degree of heart failure The range of errors in the performance of the test must be considered Moreover heart failure may be present even though the circulation time is normal or the circulation time may be prolonged when the patient is relatively free from symptoms Improvement may result from therapy while the circulation time remains unchanged For these reasons as well as because of the variations encountered in healthy subjects most of these procedures have limited practical importance in bedside cardiology Furthermore diagnosis of congestive heart failure is easier and no less exact by other means Since healthy subjects show a wide difference in the velocity of circulation the method does not permit the diagnosis of beginning or imminent heart failure

The procedure has some value however in the recognition of right to left shunts in congenital heart disease in the differentiation of bronchial and cardiac asthma (the circulation rate in the former is normal) in the localization of pericardial adhesions which compress the superior or inferior vena cava in the evaluation of how much the heart contributes to dyspnea in a patient with pulmonary emphysema and cardiac disease (pulmonary emphysema does not prolong the circulation time) and in ascertaining whether ascites is the result of cardiac failure Of theoretical interest also is the discovery of the diminished velocity of blood flow in most patients with congestive heart failure

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Chapter 7

Venous Pressure

THE CLINICAL IMPORTANCE of venous pressure became fully appreciated when it was realized that cardiac activity depends to a considerable extent upon the amount of blood returned to the heart and that this in turn depends upon the venous pressure. The veins cannot be regarded as passive tubes; their width and capacity vary continually under the influence of hormones, chemical substances such as carbon dioxide, and central and reflex (carotid sinus) nerve impulses. It is the amount of blood returning to the heart which regulates the cardiac output, rather than the converse. If the quantity of blood returning to the right heart is greater than the heart can transfer to the arterial side, venous pressure rises. Normally, venous pressure rises during exertion.

Measurement of venous pressure aids in the clinical diagnosis of right ventricular failure. Moreover, it will often help to determine whether cardiac decompensation plays a part in a case of hepatic enlargement or ascites. Likewise, determination of the venous pressure will often make it possible to learn how much the cardiac factors contribute to the clinical picture when a patient has extensive pulmonary emphysema and fibrosis.

In some cases of right ventricular failure, however, the liver may be enlarged and edema present while venous pressure is normal. In these cases the veins may be dilated, so that inspection sometimes yields more information than the determination of venous pressure, since the venous bed has adapted itself to the greater content.

Methods. Whereas a dilated vein which is not under pressure is difficult to palpate, a marked increase in venous pressure causes it to feel like a hard cord or a thrombosed vessel.

The simplest method for determining venous pressure remains the procedure originally suggested by Gaertner. This method is based on the fact that since the veins of the upper extremities communicate with the right atrium, they act like a manometer and indicate intra-atrial pressure with great exactitude. If the arm of a relaxed and seated patient is permitted to hang down for 15 minutes, the veins on the back of the hand become congested and easily visible. If the eyes of the examiner are fixed upon a small vein on the back of the hand and the arm of the patient is slowly elevated by the observer, a point will be reached at which the pressure in the hand vein exceeds the pressure in the right atrium; at this moment the vein empties and collapses. The level at which this collapse occurs is regarded as the point at which the vein is subject to the same pressure as the right atrium.

As a reference point the upper border of the fifth rib is chosen in the seated patient Normally the veins should collapse 10 cm above the reference point Sclerotic veins however do not collapse readily The observation that the venous pressure in one arm may be higher than in the other if the first has performed some work shortly prior to the test demonstrates that the values obtained with this method do not depend upon the state of the circulation alone

Sir Thomas Lewis recommended inspection of the superficial jugular veins for the estimation of venous pressure Normally these veins collapse if they are flush with the upper end of the manubrium sterni This is the reference level regardless of body position Therefore in the upright posture no portion of the vein should be visibly congested under normal conditions If the veins remain engorged above this level venous pressure is elevated and the higher this congestion extends up the neck in the erect patient the higher the pressure

As a reference level in the supine position some observers recommend a point 5 cm dorsad to the fourth costochondral junction or 10 cm above the level of the back of a patient lying on a table

The normal levels vary according to the reference point used and range from 4 to 15 cm water Some investigators regard 10 cm as the upper limit and others consider values over 15 cm as abnormal Figures of over 32 cm have been obtained in congestive heart failure Direct measurement of the pressure by means of a catheter within the human right atrium yields values of 3 to 7 cm water in normal persons

A needle introduced into a vein provides a direct method for measurement of venous pressure but this technic also suffers because of the impossibility of locating the correct zero level This and other similar methods offer little advantage over the procedures mentioned above

Interpretation While there is no parallelism between the height of the venous pressure and the degree of decompensation venous pressure is usually elevated in failure Since venous pressure is normal in uncomplicated emphysema and lung asthma this fact may aid in problems of differential diagnosis It is elevated in a compensated tricuspid stenosis and in pericardial adhesions The method is of value in the diagnosis of obstruction of the superior or inferior vena cava Following venesection venous (and spinal fluid) pressures fall

Within certain limits increased venous pressure means better filling of the heart and therefore improved cardiac efficiency in accordance with Starling s law this holds true despite the shortening of diastole by the increase of heart rate via the Bainbridge reflex In this sense it helps to compensate the heart lesion These rules are not valid when the heart has no reserve force

Of clinical interest is the phenomenon of *hepato jugular reflux* Strong pressure exerted with both hand on the right upper abdomen particularly on the patient s liver area does not change the filling of the veins of the neck in normal individuals The venous pressure remains unchanged or more often it falls 1 to 3 cm water In patients with right heart failure the veins become engorged and the venous pressure may rise by 3 cm water According to Burch and Ray increased tonus of the veins in conjunction with greater filling is responsible

of 3500 postmortem examinations but by using a more exact procedure the same authors found the condition in 14 per cent of the cases in a second series of patients (Hampton and Castleman) There is no other autopsy finding which is more readily passed over In many reports only the number of infarctions is noted the fact that pulmonary embolism often is not followed by infarction finding no consideration Whereas Belt believes that infarction occurs in somewhat more than 50 per cent of the cases of pulmonary embolism others found an infarction only in 27 to 30 per cent In another study in which pulmonary infarction was observed in 5 2 per cent of 6 048 necropsies only 22 per cent of these infarctions were diagnosed ante mortem In 60 per cent a medical disease existed (Krause and Chester) It is claimed that a pulmonary embolism appears after 3 5 per cent of major operations and in 5 3 per cent of parturitions At least every tenth embolism is said to be lethal but we would assume the incidence of death to be much rarer The danger of pulmonary embolism is greater in all patients over 50 years old especially if they are obese It is estimated that 34 000 persons in the United States die every year from this accident Fat embolism occurs after injuries Air embolism is prone to occur in connection with fractures Embolism from tumor particles is rare but does occur

Fatal pulmonary embolism may rarely develop from a thrombus in the axillary veins following diagnostic or therapeutic venipuncture

Pathology

Pulmonary Embolism Embolism may occur in the trunk of the pulmonary artery in one of its main branches or in its peripheral ramifications In a majority of instances the embolus lodges in a vessel supplying the lower lobe of the right lung This is not entirely explained by anatomic factors such as the greater width of the right pulmonary artery The location of pulmonary infarcts was recorded in a series of 200 cases with the following result 84 cases had infarction of the lower lobe of the right lung 52 showed an infarction of the lower lobe on the left 64 had infarction of both lungs (Gsell) According to the same observer infarction of an upper lobe occurs in only 10 per cent of the cases and these have a poorer prognosis Multiple rather than solitary pulmonary embolism characterizes a high percentage of cases a point of major therapeutic import

If small masses of a radiopaque substance are introduced experimentally into the femoral vein of a dog a majority of such emboli pass into the branch of the pulmonary artery supplying the lower lobe of the right lung in two experiments three out of every five emboli inserted in this way even passed into the same small artery of the right lower lobe (Scherf and Schoenbrunner)

Pulmonary Thrombosis Hemorrhagic infarction of the lung may also be the consequence of thrombosis of a pulmonary artery Fowler found thrombosis of this vessel 6 times in 935 consecutive necropsies A distinction between pulmonary thrombosis and pulmonary embolism may be difficult even at necropsy The formation of a thrombus at the site of a small embolus is also encountered A part of

the thrombus may become detached and may cause an embolism in a peripheral part of the artery Often a thrombus forms at the site of sclerosis of a pulmonary artery Pulmonary thrombosis is also encountered in the postoperative or post partum period and is common in conjunction with disease of the pulmonary or mitral valve Since such thrombi ordinarily are terminal developments the symptomatology tends to be masked by the underlying disorder Dyspnea and cyanosis stand in the foreground of the clinical picture while the stormy manifestations of pulmonary embolism are often absent

Pulmonary Infarction Since pulmonary embolism often is not followed by hemorrhagic infarction an accurate postmortem estimate of its incidence would require a technic similar to that used to discover coronary occlusion namely radioscopic examination after the injection of an opaque substance into the pulmonary artery The formation of a hemorrhagic infarct is greatly enhanced by the presence of pulmonary congestion this may account for the high incidence in cardiac patients In the experimental animal hemorrhagic infarcts appear after ligation of the pulmonary arteries *and* veins

Hemorrhagic infarction of the lung may have other causes Thus infected emboli formed in the course of a general sepsis cause capillary damage and hemorrhagic infarction Embolism of a large pulmonary artery or embolism in old people causes hemorrhagic pulmonary infarction Anemic infarction of the lung is uncommon

Pulmonary embolism leads to localized hyperemia and edema The hemorrhagic infarct is a solid well defined conical mass whose apex extends toward the hilus The base of the infarct is almost invariably formed by the pleura so that pleural irritation is inevitable Around the infarct is a zone of reactive inflammation just as it develops in the myocardium after infarction The alveoli are filled with blood which may be fresh or disintegrated depending upon the age of the infarct Unlike a cerebral apoplexy the pulmonary parenchyma is not destroyed by a hemorrhagic infarct and the red blood cells are slowly absorbed If the patient survives there may be complete healing without evidence of necrosis and the site of a former infarction may be visible on x ray films only as a fine scar a small pleural adhesion may be the sole evidence of a previous pulmonary infarction

Hemorrhagic infarctions heal slowly Eighteen months may be required before canalization is complete or the scar forms Encapsulation and cicatrization are not unusual but the formation of pulmonary cysts after infarction is rare If the patient survives embolism of a large pulmonary artery canalization may follow The ensuing arterial stenosis may lead to secondary thrombosis

Symptom

Massive and Small Embolisms Occlusion of the main stem of the pulmonary artery by an embolus causes almost instantaneous death and scarcely requires detailed comment Sometimes the patient has only time to cry out in alarm If

death is delayed for a few minutes the syndrome of sudden asphyxia marked anxiety cyanosis and finally loss of consciousness is most dramatic

Massive embolism of one large pulmonary artery multiple embolisms of smaller vessels or a solitary embolism of a small peripheral lung artery may produce a very similar picture Accordingly one should not infer that massive embolism has occured merely because the subjective phenomena are severe As a matter of fact even massive pulmonary embolism causes remarkably few symptoms at times This is understandable since the clinical picture in most cases does not derive from the mechanical obstruction of the pulmonary vessels

Dyspnea One of the most common symptoms is dyspnea of sudden onset It may be mild or extreme — in the latter instance it requires immediate treatment The sudden occurrence of dyspnea in a cardiac patient particularly a bed ridden one arouses the suspicion of a pulmonary embolus provided no other explanation is satisfactory This dyspnea is subjective and objective Breathing is rapid often shallow and is associated with great apprehension or even extreme anxiety For the most part the dyspnea is of reflex origin but massive embolism will cause dyspnea without the activation of reflexes Pulmonary edema occasionally occurs and causes dyspnea Dyspnea may be the only symptom of pulmonary embolism Experimentally it occurs even when small arteries are occluded and disappears immediately if the vagi are severed If reflex bronchospasm develops as occasionally happens the breathing may be asthmatic

Pain Pain is a common symptom of pulmonary embolism Four types can be distinguished

(1) Pain may be felt in the precordium or in the retrosternal area and may present all the features of pain from a myocardial infarction The pain may be mild or excruciating it may last for hours and like the pain of coronary occlusion it may radiate into the arms As will be shown later the distinction between pulmonary embolism and myocardial infarction may be extremely difficult In a series of 100 cases of the former there was a history of pain in 32 instances In another report pain in the chest or back was mentioned in 50 per cent of the cases (Moller) This pain may occur without any changes appearing in the electrocardiogram At least in some patients this pain may be due to a similar mechanism as that observed in patients with high pressure in the lesser circuit (see chapter on Cor pulmonale)

(2) Sometimes anginal pains recur at short or long intervals during the first twenty four hours The pain experienced may last for only a few minutes and may radiate to the ulnar side of the left or right arm Nitroglycerin brings prompt relief (Scherf Currens and Barnes)

(3) Hours or days after pulmonary embolism pain may develop in the right or left side of the chest It is aggravated by deep breathing The pain is typical of pleuritis this diagnosis being confirmed by the appearance of a friction rub over the involved area

(4) A constant pain may be referred to the shoulder neck abdomen or lumbar region It lasts usually for days The common occurrence of this kind of pain and the frequency with which it is misinterpreted is worthy of emphasis Presumably the pain results from diaphragmatic pleurisy The great incidence of pulmonary infarction at the base of the right or left lung makes irritation of the diaphragmatic pleura a common event The center of each leaf of the diaphragm is innervated by the phrenic nerve which is derived from the cervical segments inflammation of the dome of the diaphragm therefore causes pain which is referred to the cervical region Experimental irritation of the central portion of the diaphragm actually causes pain which is referred to the neck and shoulder corresponding to the third and fourth cervical segments (Capps and Coleman) These patients are often treated for arthritis Likewise after gynecologic operations the pain is falsely attributed to the pressure of shoulder pads while the patient is in the Trendelenburg position Since the costal or marginal portion of the diaphragm receives afferent nerves from the last six thoracic nerves irritation of this section evokes pain that seems to arise in the lower part of the thorax the upper abdomen or the lumbar region

For this reason patients with pulmonary infarction may be suspected of acute appendicitis or cholecystitis and as personal experience has repeatedly confirmed this has often led to unnecessary laparotomy Since strong stimuli cause muscular rigidity tenderness and hyperesthesia of the corresponding segments the danger of an erroneous diagnosis is great

Irradiation of pain to other segments and even to the opposite side may occur If autonomic stimuli irradiate reflex visceral spasm and even paralytic ileus may develop in connection with pulmonary embolism (see next chapter)

Sometimes pain is felt later over the precordium when pericarditis supervenes (see below)

Hemoptysis The diagnostic importance of hemoptysis in pulmonary embolism is overestimated for it actually occurs only in a minority of cases Hemorrhagic sputum cannot occur unless a hemorrhagic infarct develops and is infrequent even when necropsy discloses several old and recent hemorrhagic infarctions When present hemoptysis undoubtedly facilitates the diagnosis Sometimes only close inspection of the sputum reveals the presence of fine streaks of blood but in other cases the expectoration is definitely red and mucoid It is never frothy as in pulmonary edema usually it is very tenacious and adheres to the sides of the container Profuse hemoptysis occurs at times

The appearance of bloody sputum in a cardiac patient does not prove the existence of pulmonary infarction If the usual causes prevailing in noncardiac patients can be eliminated and an aortic aneurysm is ruled out pulmonary congestion may be provocative Hemoptysis from pulmonary engorgement is by no means uncommon and patients with mitral stenosis were sometimes sent by mistake to a sanatorium for the treatment of a nonexistent pulmonary tuberculosis Hemoptysis may also occur in coronary thrombosis and in paroxysmal tachycardia

Other Symptoms

Patients with pulmonary infarction may display great anxiety Not infrequently the body is bathed in a cold sweat Csell reported chills in one per cent of his cases Loss of consciousness occurs and is related to the fall of blood pressure A feeling of impending death is not rare

On rare occasions we have noted painful swallowing This pain was felt in the interscapular region and occurred when food passed through the esophageal hiatus When severe it created feeding problems Diaphragmatic pleurisy or periesophagitis has seemed to be the most likely causative factor A similar lesion may initiate persistent and exhausting hiccough

Signs

Temperature and Heart Rate The most consistent and thus the most important signs are elevation of the temperature and the heart rate Formerly both were regarded as evidence of venous thrombosis and have been called the signs of Mahler and Michaelis However it is not established that a simple thrombosis without thrombophlebitis provokes fever and tachycardia Embolisms are probably provocative

Every unexplained rise of temperature and heart rate in a cardiac patient as well as a postoperative patient should arouse the suspicion of pulmonary embolism The pulse rate may increase considerably and a tachycardia of 180 beats per minute may be reached in pulmonary embolism The fever subsides in 4 to 5 days by gradual lysis a renewed elevation of temperature suggests the development of a complication or a new embolism

Cyanosis and Jaundice Azotemia Cyanosis may be very pronounced but is often absent despite marked dyspnea Jaundice is a common finding As mentioned previously the combination of hemolysis and hepatic damage in a cardiac patient often causes jaundice The discoloration may be rather deep and may last for weeks A similar jaundice is encountered occasionally in hemorrhage with marked anemia leading to hepatic damage (ruptured ectopic pregnancy) For a long time the hemorrhagic infarct was regarded as a site for the extrahepatic formation of bile pigment

In some cases of pulmonary infarction with jaundice the nonprotein nitrogen of the blood serum reaches a level of more than 60 mg per cent coincidentally with a high value for serum bilirubin (Csell)

Examination of Lungs If the infarct is large examination of the lungs may reveal dullness of varying intensity and crepitant rales over circumscribed areas Since embolism occurs most often in the lower lobe of the right lung this area should be examined with great care On the other hand examination may fail to reveal any abnormality despite embolism and infarction often the affected area is too remote from the thoracic wall to create signs If physical signs are discovered they need not be due to infarction per se but rather to a complicating process like infarction pneumonia

A pleural effusion often forms most commonly on the right side It develops in 40 to 50 per cent of patients with pulmonary embolism In 100 cases of pleural effusion which appeared following infarction fluid developed on the right side in 51 on the left in 28 and bilaterally in 21 The fluid may possess the characteristics of an exudate and frequently is hemorrhagic Often a pleural friction rub is audible but no effusion develops Pleural irritation is common since every infarction of necessity reaches the surface of the lung

Cardiac examination reveals the tachycardia mentioned above Paroxysmal atrial fibrillation is a rare event presumably caused by acute dilatation of the right atrium with stretch of the muscular fibers (Scherf et al) Cardiac enlargement is rare unless it was present prior to the infarction or multiple infarctions (embolisms) had occured over a long period If pre existing disease has caused cardiac enlarge ment after an infarction dullness may rapidly develop to the right of the sternum as the result of right atrial dilatation The second pulmonic sound is often accen tuated and a systolic murmur may be heard over the pulmonary artery for a few hours this bruit is sometimes called Litten s murmur although it was mentioned by Laennec Gallop rhythm is not rare

A syndrome which may lead to a remarkable dilatation of the right heart is is known as subacute cor pulmonale In patients demonstrating this syndrome because of the large heart with gallop rhythm and evidence of congestive failure the diagnosis of intrinsic heart disease is made and eventual pulmonary x ray findings are explained by the diagnosis of pneumonia This picture is seen in repeated embolization of the lungs in which therapy with anticoagulants or venous ligation often are helpful

The pericarditis occurring in a small percentage of cases apparently represents an extension from the pleurisy by continuity the mechanism is the obverse of the pleuritis which develops in the left chest after the pericarditis of myocardial infarction The pericardial friction rub may persist for a few days Occasionally pleuropericardial friction sounds are heard along the left border of the heart Disturbances of rhythm such as paroxysmal atrial fibrillation can occur as men tioned above Finally there may be a fall of blood pressure in some instances reaching shock levels

Laboratory Investigations Leukocytosis of 10 000—15 000 is found in the average case but the figures may be much higher and with an infarction pneu monia the count may reach 45 000 with predominantly polymorphonuclear cells The erythrocytic sedimentation rate rises and undergoes further acceleration if a pulmonary complication supervenes

Roentgenology may contribute to the diagnosis of pulmonary infarction The typical wedge shaped shadow with its apex directed toward the hilus and the broad base at the pleural surface is not very common More often the shadow is round because its location and projection on the chest plate determine the shape If films are taken in different positions it may be possible to discover additional infarcts The infarction shadow may persist as long as two or three months therefore particularly if there are several infarcts in the same lung the radiologic

Other Symptoms

Patients with pulmonary infarction may display great anxiety Not infrequently the body is bathed in a cold sweat Gsell reported chills in one per cent of his cases Loss of consciousness occurs and is related to the fall of blood pressure A feeling of impending death is not rare

On rare occasions we have noted painful swallowing This pain was felt in the interscapular region and occurred when food passed through the esophageal hiatus When severe it created feeding problems Diaphragmatic pleurisy or pericsophagitis has seemed to be the most likely causative factor A similar lesion may initiate persistent and exhausting hiccough

Signs

Temperature and Heart Rate The most consistent and thus the most important signs are elevation of the temperature and the heart rate Formerly both were regarded as evidence of venous thrombosis and have been called the signs of Mahler and Michaelis However it is not established that a simple thrombosis without thrombophlebitis provokes fever and tachycardia Embolisms are probably provocative

Every unexplained rise of temperature and heart rate in a cardiac patient as well as a postoperative patient should arouse the suspicion of pulmonary embolism The pulse rate may increase considerably and a tachycardia of 180 beats per minute may be reached in pulmonary embolism The fever subsides in 4 to 5 days by gradual lysis a renewed elevation of temperature suggests the development of a complication or a new embolism

Cyanosis and Jaundice Azotemia Cyanosis may be very pronounced but is often absent despite marked dyspnea Jaundice is a common finding As mentioned previously the combination of hemolysis and hepatic damage in a cardiac patient often causes jaundice The discoloration may be rather deep and may last for weeks A similar jaundice is encountered occasionally in hemorrhage with marked anemia leading to hepatic damage (ruptured ectopic pregnancy) For a long time the hemorrhagic infarct was regarded as a site for the extrahepatic formation of bile pigment

In some cases of pulmonary infarction with jaundice the nonprotein nitrogen of the blood serum reaches a level of more than 60 mg per cent coincidentally with a high value for serum bilirubin (Gsell)

Examination of Lungs If the infarct is large examination of the lungs may reveal dullness of varying intensity and crepitant rales over circumscribed areas Since embolism occurs most often in the lower lobe of the right lung this area should be examined with great care On the other hand examination may fail to reveal any abnormality despite embolism and infarction often the affected area is too remote from the thoracic wall to create signs If physical signs are discovered they need not be due to infarction per se but rather to a complicating process like infarction pneumonia

wave in one of the leads We have seen tracings in which the QRS complexes alone underwent the modifications just mentioned whereas the PS T segments and T waves remained normal (Scherf and Boyd) The differentiation between a posterior inferior wall infarction and pulmonary embolism is not always easy in the early stage but usually it becomes possible in the following days The inversion of the T waves in the chest leads in positions 2 and 3 does not occur with inferior wall infarction causing a deep Q wave and an elevated RS T with an inverted T in lead III There are no changes in aVF characteristic for inferior infarction In cardiac infarction no S wave appears suddenly in lead I to disappear

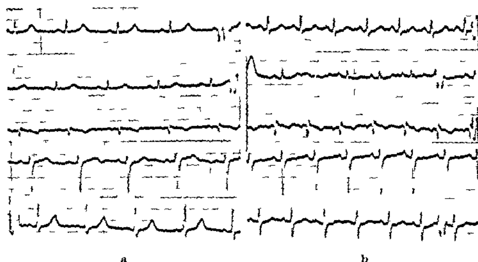


FIG 19 (a) The electrocardiogram taken preoperatively is normal (b) The electrocardiogram recorded 6 days after an appendectomy shows the typical signs of a pulmonary embolism in addition to a sinus tachycardia a deep S wave appeared in I and the Q wave is deeper in III The T wave in V 2 is slightly inverted it is lower in V 5

within a few days it is common in pulmonary embolism The electrocardiographic changes in pulmonary embolism usually persist for several days in one of our patients they remained for three weeks A small pulmonary embolus is capable of inducing electrocardiographic changes in the experimental animal The electrocardiographic changes may be found without clinical signs of pulmonary embolism and there is no parallelism between the extent of alteration in the electrocardiogram and the symptoms

Figure 19 shows a common pattern The electrocardiogram of a 48 year old man had been taken preoperatively (figure 19a) and showed essentially normal findings Six days after a successful appendectomy clinical symptoms and signs of a pulmonary embolism suddenly occurred The electrocardiogram (figure 19b) showed in addition to the increase of rate the appearance of a typical S wave in lead I which we always consider the most characteristic finding Simultaneously the Q wave in lead III became deeper The T wave in V 2 is slightly negative the

T wave in V5 is lower The other changes are readily explained by the increased rate

The changes in V2 speak against the diagnosis of an inferior wall infarction

Complications

If the patient survives the initial shock recovery usually is rapid and the danger is over in a few days However there is always the threat of a new embolism Moreover if certain complications develop the prognosis is guarded

Infarction pneumonia is a common complication In addition to the reactive inflammation surrounding the infarcted area in all patients with hemorrhagic infarction pneumonic patches appear The temperature curve undergoes a sudden rise and the systemic signs of pneumonia are present Rarely the infarcted or necrotic area becomes infected with pyogenic or putrefactive organisms so that a pulmonary abscess or gangrene occurs particularly in debilitated patients A pulmonary cavity or empyema may result from an aseptic necrosis

In cardiac patients the strain imposed on the right heart by emboli m may lead to marked hepatic enlargement and to right heart failure The latter may be resistant to therapy Not rarely new emboli appear again and again over a long period of time causing progressive right heart failure with marked cyanosis and dyspnea even in the otherwise healthy person Symmetrical peripheral gangrene has been observed although rarely (Hejtmancik and Bruce)

Differential Diagnosis

Most of the conditions with which pulmonary embolism and infarction may be confused were mentioned in the preceding paragraphs The clinical differentiation between coronary thrombosis and pulmonary embolism sometimes is extremely difficult Both conditions may be associated with severe prolonged retrosternal pain followed by a fall of blood pressure fever leukocytosis dyspnea tachycardia pulmonary signs increased sedimentation rate and electrocardiographic changes Even hemoptysis occurs in both while in some cases the existence of a lung infarct can be established Sometimes the differentiation is impossible without the electrocardiogram

The resemblance to acute abdominal conditions such as appendicitis or cholecystitis was mentioned earlier Pneumonia also causes an abdominal syndrome and the provocative mechanism is probably similar The picture of a paralytic ileus may be caused by pulmonary embolism The diagnosis of virus pneumonia or hypostatic pneumonia is often wrongly made while in other cases bronchogenic carcinoma or atelectasis is diagnosed

The responsibility of pulmonary embolism for the appearance of a bronchopneumonia may be overlooked and a distinction between infarction pneumonia and virus pneumonia may be difficult By the same token simple pleuritis may be diagnosed and the provocative infarction may remain undiscovered

Pathologic Physiology

Embolism in the main stem or in a major branch of the pulmonary artery may cause death almost instantaneously. In other patients sudden severe dyspnea, anxiety and pain are succeeded by unconsciousness and death in a short time. Autopsy reveals a small embolism. There are patients, however, who survive an embolism in one of the main pulmonary arteries.

Reduction of the pulmonary circulation to less than 50 per cent does not necessarily produce pressure changes in the systemic or lesser circulation, and ligation of a major pulmonary artery during a thoracic operation ordinarily does not have serious consequences. Fatalities or very severe manifestations may occur, on the other hand, when a very small embolus lodges in the periphery of the lung. For example, Sauerbruch mentions a 32 year old patient who died suddenly after a herniotomy. At post mortem nothing was found except a small embolus 3 mm. in width in a minor artery within 4 cm. of the lung surface. In another study of 35 fatalities caused by pulmonary embolism, the embolus was small in seven.

These observations alone imply that the mechanical occlusion of the pulmonary vessel is not the sole reason for the serious effects of lung embolism.

To explain the marked disturbances following embolism of a small pulmonary artery, recourse was often made to nervous (vagal) cardiac inhibition and to shock. Even vagal reflexes were incriminated. However, shock is often absent despite other serious symptoms, and it is difficult to understand the theory of vagal inhibition since a tachycardia usually prevails; moreover, a direct vagal influence on the mammalian ventricle does not exist or is negligible.

Recent experience indicates that certain reflex mechanisms play a major part in the development of circulatory disturbances in pulmonary embolism. These reflexes may be divided into three groups: (1) intrapulmonary, (2) those from the pulmonary vessels to the systemic circulation, and (3) pulmocardiac (pulmocoronary) reflexes.

Intrapulmonary Reflexes. Many experimental, pathologic and clinical observations demonstrate how pulmonary embolism imposes increased strain on the right ventricle. The dilatation of the right ventricle and pulmonary artery, the accentuation of the second pulmonic sound and the systolic murmur over the pulmonic area speak in favor of larger demands upon the right ventricle. The dilatation has been seen in experimental animals and in man. The outflow tract is primarily involved, as would be expected in a dilatation due to increased strain. This acute rise in intrapulmonic pressure leads to the appearance of an "acute cor pulmonale." Massive pulmonary embolism certainly may cause such changes, although extensive reduction of pulmonary circulation to 50 per cent of normal by ligation of the main right or left pulmonary artery or even obstruction of many pulmonary vessels by embolism need not create any alteration in the pulmonary arterial pressure. On the other hand, the intrapulmonic blood pressure may increase with a small peripheral embolism of one pulmonary artery.

The part played by reflexes in causing this rise of pressure in small peripheral embolism is easily understood if we recall the situation that prevails when a peripheral artery (an artery of the leg, for example) is occluded by an embolus. In such a case rather stormy manifestations are common. The leg may be bloodless, cold, pale and immobile; tendon reflexes vanish and even sensation is severely disturbed. The situation appears to be one in which the femoral artery had been occluded. After some time, during which papaverine and other vasodilators are administered, rapid improvement may occur. Naturally the embolus is not removed by drugs of this type; rather, there is the potential danger that because of the disappearance of vascular spasm the clot might be thrust toward the periphery where the collateral circulation is even less adequate. It seems more plausible to assume that occlusion of a small peripheral artery, as small as a muscular branch of an interosseal artery, for example, causes a reflex vasoconstriction of neighboring vessels; this spasm could produce the alarming syndrome which promptly disappears after the administration of vasodilators. The existence of a reflex vasoconstriction following irritation of peripheral arteries and veins is established, and arterial spasm in thrombophlebitis is common. Axon reflexes are responsible for this phenomenon.

Conceivably a similar reflex spasm operates in pulmonary embolism, which may elevate the pressure in the lesser circuit. The rich innervation of the lung and the existence of adrenergic pulmonary vasoconstrictor fibers make such reflexes possible.

Reflexes from the Lung to the Systemic Circulation. Increase of pressure in the lesser circuit causes a reflex bradycardia and a fall of systemic blood pressure. The reflex is released from the receptors in the pulmonary arteries and disappears if the pulmonary nerves are cut.

This reflex has been called protective, since it prevents overdistension of the lesser circuit by dilating the systemic vessels. The early bradycardia observed in some patients with pulmonary embolism as well as the shocklike syndrome with marked fall of blood pressure may be caused by such a reflex mechanism (Schwiegk).

Reflexes from the Lung to the Coronary Arteries. The study of patients with pulmonary embolism who showed gallop rhythm and marked changes in the electrocardiogram but no dilatation of the right heart during life or at post mortem and no evidence of organic heart disease led to the following hypothesis (Scherf). A pulmocoronary reflex from the site of the embolus in the pulmonary artery or from the infarcted area causes the coronary arteries to narrow and leads to anginal pain, electrocardiographic changes, and even to death. There need be no actual coronary artery constriction. The signs and symptoms could be explained by the tachycardia and increased load of the right ventricle without a corresponding increase in the blood supply to the heart. This would lead to hypoxia, especially in the most sensitive areas around the papillary muscles subendocardially. The existence of reflexes from the lung and other parts of the respiratory tract to the heart is indisputable (many examples will be cited in the next chapter). The powerful influence of reflexes arising in the lung and

on the heart becomes clear to every physician who has observed patients (1) with attacks of paroxysmal atrial tachycardia which do not respond to different vagal reflexes including carotid pressure but are promptly stopped when the patient inspires deeply or (2) who developed paroxysmal atrial flutter or fibrillation whenever they took a deep breath Against the assumption that all findings *in pulmonary embolism can be explained solely by increased pressure in the lesser* circuit and in favor of the theory just advanced the following facts are cited

(1) Fatalities from pulmonary embolism occur in otherwise healthy patients who present gallop rhythm and similar symptoms without signs of increased pressure in the lesser circuit It also occurs when there is no right ventricular strain during life and no evidence for this at post mortem (figure 18)

(2) The attacks of angina pectoris in particular those attacks which respond to nitroglycerin are best explained by a myocardial ischemia

(3) In cases of pulmonary embolism the electrocardiogram shows not only the changes one would anticipate in right ventricular strain but also the alterations expected in ischemia of certain parts of the myocardium This has been re emphasized by Meyers in his recent book on the unipolar electrocardiogram The depression of the RS T in lead I the inversion of the T wave V2 and V3 and the elevated RS T in aVL speak for interference with the circulation in the right coronary artery

(4) The electrocardiographic changes of pulmonary embolism are not reproduced experimentally by increasing pressure in the lesser circuit e g by clamping the pulmonary artery

(5) Occasionally the changes in the electrocardiogram persist for weeks The increase of intrapulmonic arterial pressure lasts only for a few hours and the systolic murmur over the pulmonic valve area is equally transient

(6) The electrocardiographic changes often do not present a typical pattern whereas those evoked by right or left ventricular strain show constant features

(7) Acute right ventricular strain resulting from pneumothorax prolonged bronchial asthma and the like does not produce these changes in the electrocardiogram

(8) Occasionally patients have an electrocardiogram very similar to that observed in acute inferior *wall infarction Even in clinical instances* in which the right ventricle works under greater strain and there is a tachycardia and a decreased oxygen saturation of the blood the pattern of acute infarction does not appear in the electrocardiogram

(9) The presence of necroses in the myocardium especially in the wall of the right ventricle in patients dying from a small pulmonary embolism in the absence of organic coronary artery disease suggests a disturbance of the coronary circulation Moreover these necrotic areas have peculiarities of form and position which are found whenever the myocardium works under hypoxic conditions

(10) The occurrence of paralytic ileus or gastrointestinal phenomena in pulmonary embolism likewise speaks in favor of irradiating autonomic reflexes

Aviado and Schmidt reviewing reflexes from stretch receptors in heart and lungs mention unpublished experiments by Niden that demonstrate the existence of axon reflexes in the lung One lobe of the dog s lung was supplied with blood from a donor dog Injection of glass beads into the arteries of an unperfused lobe caused reflex vasoconstriction in the perfused lobe even after the vagus nerves were cut Similarly we invoked axon reflexes for many years therefore the experimental findings of Malinow et al showing persistence of electrocardiographic changes after the vagus nerves in the neck were cut do not conflict with our explanation

Hochrein and Schneyer measured the blood flow in the coronary arteries directly and found in the right coronary artery a diminution of the blood flow following experimental pulmonary embolism Hackel et al saw a marked rise of pulmonary arterial pressure (almost three times the normal pressure) after intravenous injection of a suspension of lycopodium There were no significant changes of the coronary blood flow This alone should create myocardial hypoxia since with the greater activity of the heart an *increase* of blood flow should be needed

Comroe et al discuss the possibility that 5 OH tryptamine (serotonin) formed in blood clots by dissolved platelets (which given intravenously to cats causes not only reflex bradycardia hypotension and apnea but also pulmonary vasoconstriction and bronchospasm) is responsible for some of the signs and symptoms discussed above

Because the existence of many of the e reflexes remains undemonstrated in the experimental animal they are discarded by some physiologi ts Our inability to reproduce them however does not mean they do not exist It is not possible to reproduce many of the well recorded reflexes mentioned in the next chapter Even though it is scarcely possible to prove experimentally that gentle mechanical irritation of the rectum can cause paroxysmal ventricular tachycardia or fibrillation this undoubtedly is what happens in man under particular circumstances It will also not be easily proven experimentally that mechanical irritation of the pharynx can lead to cardiac standstill although this too probably has often occurred (but again only with a particular constellation of factors — see next chapter)

It is difficult to decide whether the reduction of coronary artery blood flow alone or the augmented strain on the right heart with unfulfilled increased requirements for oxygen is responsible The second possibility has greater appeal Experimental investigation of this problem is fraught with difficulties since these reflexes are not active in every individual (this also will be discussed in the next chapter)

Before discussing the treatment of pulmonary embolism we deem it appropriate to give a short description of the chief initiating process venous thrombosis This seems in order at least insofar as cardiac patients are concerned

Venous Thrombosis and Pulmonary Embolism

Usually pulmonary embolism is caused by thrombi from the pelvic veins or from veins in the lower extremities. Intraatrial thrombi, formerly regarded as very important, are rarely provocative.

In one of the first systematic investigations of the occurrence of venous thrombosis the condition was found in the calf veins in 27.1 per cent of 324 consecutive postmortem examinations in a general hospital (*Poessle*). In many cases the femoral veins were also affected. In another study in which the small veins of the foot were included in the investigation, venous thrombosis was found in 60 per cent of 165 non selected subjects. In 52 instances the thrombosis was bilateral. Thrombosis of the plantar veins usually involves the vessels of both feet and is often the primary site; the thrombosis of the calf veins is often secondary. This thrombosis is more common in patients with fallen arches. In 100 patients with venous thrombosis of the lower extremities, the calf veins were affected in 87, the plantar in 71, and the veins of the thigh in 22 (Neumann). In this series pulmonary embolism had occurred in 11.8 per cent. In another investigation venous thrombosis in the leg was found in 52.7 per cent of 351 autopsies (Hunter et al.). Medical cases comprised 79.7 per cent of the series. If the veins of the pelvis as well as those of the extremities had been investigated, the incidence of venous thrombosis would have been even greater. In a statistical study of 1665 cases of postoperative pulmonary embolism that included 135 fatalities, clinical as well as necropsy evidence of a venous thrombosis was missed in 24.3 per cent (Barker et al.). Presumably the whole thrombus detached itself to form the embolus. For unknown reasons thrombosis occurs more often in the veins of the left lower extremity than the right one.

Accordingly, the disease is much more common than formerly believed. The clinical diagnosis is difficult and often impossible, especially when the phlebothrombosis is bland and without much inflammatory reaction (thrombophlebitis).

A common condition is the one known as traumatic thrombosis, that is, a venous thrombosis that occurs several hours or days (up to 14 days) after blunt trauma, striking the leg against a chair or stumbling against the bumper of an automobile. The trauma may be so slight that patients forget it completely, making the subsequent thrombosis seem "spontaneous."

"Effort thrombosis" follows an unusual effort and often occurs in the veins of the arms following backward rotation. It has been described particularly in tall men after severe effort (Naide). Effort with or without rupture of muscle fibers may locally increase venous pressure so that small veins burst and a propagating thrombosis ensues.

Venous thrombosis was often observed during the "blitz" in England when patients were seated for hours on crudely built seating devices with cross bars compressing the leg veins (shelter legs). Keeping the legs bent (a pillow under the knees) while lying quietly in bed for hours is a prolific source of thrombosis, the

Gatch frame used in many hospitals to keep the knee and hip joint bent is another device that hastens thrombus formation

One may assume that during prolonged rest the weight of the leg compresses the thin walled veins and causes a lesion of the endothelium which leads to thrombosis

In cardiac patients who often suffer from congested peripheral veins and who have an abnormally nourished vascular endothelium bed rest is frequently enforced thereby often causing thrombosis in the veins of the lower extremities

An increased tendency to thrombosis has been found in patients with congestive heart failure following rapid diuresis induced by too energetic therapy It is apparently not an increased concentration and viscosity of the blood but the movement of tissue fluid into the blood stream which is responsible

Polycythemia enhances thrombus formation

Increased coagulability has also been described following the administration of large doses of digitalis and the administration of quinidine sulfate and penicillin Even fear and apprehension are said to promote coagulation of the blood The shortening of the clotting time by a fatty meal is still under investigation

While local pain fever chills redness swelling and increased temperature in the involved area characterize some cases of thrombophlebitis venous thrombosis often presents either no local signs or else merely a slight enlargement of the calf or ankle detectable only by careful measurement Pain in the plantar area is in our opinion one of the earliest signs to indicate a beginning thrombosis in the leg (Payr) The pain appears at the mesial aspect of the plantar region due to pressure of the thrombosed veins on the nerves (Denecke) Likewise of value although often absent is the appearance of soreness of the gastrocnemius region on dorsiflexion of the foot (Homan) Pain in the calf that comes with walking in low heels (slippers) is occasionally an early sign Compression of the calf by a blood pressure cuff with pressures between 60 and 150 may cause pain (Lowenberg)

The danger from noninfected latent and unrecognized thrombosis is greater than from an obvious thrombophlebitis in which the thrombus adheres firmly to the wall of the vein

Thrombosis may develop very early in postoperative and bedridden medical patients and pulmonary embolism may occur in less than 24 hours Venous thrombosis and to a greater extent lethal pulmonary embolism become increasingly dangerous in older age groups

Of great therapeutic importance is the finding that a thrombus older than 3 days is not detached Some organization of the thrombus is seen after 24 hours

Elastic stockings are applied while the patient is bedridden and always applied for 2 to 3 months or longer when the patient is ambulatory

Prevention and Treatment of Peripheral Vein Thrombosis

Therapy begins with measures to avoid peripheral vein thrombosis To accomplish this in postoperative cases walking is recommended as early as possible although some doubt exists as to the efficacy of this measure (de Bakey)

The same procedure should be followed in cardiac patients In the first edition of this book (1935) therefore it was recommended that cardiac patients with certain exceptions (such as those with coronary thrombosis) should not be kept too quiet in bed Movement of the lower extremities was suggested even for patients with acute myocardial infarction In decompensated cardiac patients enforcement of strict bed rest seems to lead almost invariably to venous thrombosis and to the danger of pulmonary embolism No harm is done in ordinary congestive heart failure if a patient is permitted to walk from one room to another to have bath room privileges or to sit in a chair Lethal pulmonary embolism has been precipitated many times simply because such patients were forced to rest Therefore in our wards absolute bed rest for this group of patients has been prohibited during the last thirty years and the results have been encouraging Recent papers by others (Dock) stress the danger of absolute bed rest and the value of this procedure It has been stated that the rarity of pulmonary embolisms in paraplegics indicates that absolute bed rest is not dangerous (Cook and Lyons) However the immobility of such patients also prevents dislodging of thrombi

The lower end of the bed should be raised so that the legs and pelvis are elevated sufficiently to promote the return of blood to the heart The toes should be moved frequently and active or passive bending of the knees in bed should be encouraged Application of elastic bandages compresses the superficial veins and enhances the blood flow in the deep veins where thrombosis is common

Surgical intervention has found increasing popularity In recent years however the incidence of embolism in patients whose femoral veins were ligated was found to be so high and the propagation of thrombi in the pelvic veins proved so common that surgery has been almost abandoned Ligation of the inferior vena cava is rarely done since it is a more formidable procedure Furthermore a statistical study from the Massachusetts General Hospital showed that the incidence of pulmonary embolism did not diminish after the widespread employment of venous ligation Nevertheless we have repeatedly observed a complete change of the clinical picture after patients with subacute cor pulmonale caused by repeated emboli in the lung over many weeks had a ligation of the vena cava inferior performed This operation can be life saving when anticoagulant therapy is contraindicated

Since the introduction of treatment with anticoagulants the danger of pulmonary embolism following venous thrombosis or thrombophlebitis has apparently been lessened Some claim that judicious use of these agents reduces the risk of this serious complication to less than 1 per cent Others are doubtful whether the danger of thromboembolism is markedly lessened (de Bakey) To be sure the new danger of hemorrhage is added However if all rules and contraindications are observed it is worthwhile to take the risk

Heparin Heparin is a mucopolysaccharide resembling chondroitin sulfuric acid which is found in cartilage It is said to diminish the tendency of the platelets to agglutinate and it retards the conversion of prothrombin into thrombin Its mode of action is unknown Heparin is commercially prepared from beef lung

It is found in the granules of the mast cells in the body The chemical structure has not been precisely determined and therefore its synthesis has not been accomplished The standardization of heparin in different countries is not the same and consequently 50 or 100 mg is not a uniform dose One of its greatest handicaps is the fact that oral administration produces no effect

Signs of allergy have become infrequent after foreign proteins were eliminated from commercial preparations They do occur however and fever is an out standing finding

The effect of heparin is controlled by the estimation of coagulation time which although it seems to be a simple determination (Lee White method or others) is actually difficult and often inaccurate great variations are obtained if the estimation is not done very meticulously One should try to maintain a coagulation time which is two or three times the normal value but not longer than 30 minutes

Ulcers in the gastrointestinal tract hemorrhagic diathesis blood dyscrasias excessive hypertension old age (over 65 years) liver renal or pancreatic damage and subacute bacterial endocarditis are contraindications to its use Heparin is inadvisable in thrombosis of the mesenteric vessels where the tendency to bleeding is great Bleeding due to pulmonary infarction is not a contraindication

Heparin should be employed as soon as the diagnosis of a venous thrombosis is made when signs of a thrombophlebitis or of pulmonary embolism are found The recommended doses vary If given by intravenous infusion 200 mg are added to 1000 ml of physiologic saline or of 5 per cent dextrose solution and the number of drops infused per minute is adjusted to the results of tests of the coagulation time Another widely used method is to give 50 mg intravenously every 4 to 6 hours or concentrated heparin (100 mg) intramuscularly or sub cutaneously twice daily The doses are not repeated when the coagulation time is over 30 minutes If this intermittent method is used the coagulation time returns to normal between the peaks that is before the next injection is given Clinical experience has shown that these peaks suffice to prevent thrombosis even during the hours when coagulation is normal It seems that these peaks do not bring the danger of hemorrhage

While Scandinavian investigators find that the estimation of coagulation time is not necessary when heparin is administered in this way it is safer to check the coagulation time twice daily for the first few days in order to increase the dose when the patient is a hyporeactor or to decrease it when he responds too strongly

In venous thrombosis pulmonary embolism or thrombophlebitis this therapy is continued for 5 to 10 days the last injections being given when the patient is ambulatory Because of the rebound phenomenon it is advisable to diminish the dose gradually and not to stop the administration of the drug abruptly

In order to prevent postoperative thrombosis and embolism heparin is given from the second postoperative day until the patient is ambulatory

Hemorrhages in the form of hematuria, hemarthrosis, subcutaneous or intramuscular hematoma, hemopericardium appear in about 2.2 per cent of treated cases. If evidence of hemorrhage appears and an intramuscular or intravenous injection of heparin has been given shortly before, its absorption should be slowed down with an ice bag. Blood transfusions help. The intravenous injection of 50 to 100 mg. of protamine sulfate or toluidine blue (an azo-dye) in the amount of 2 mg. per kilogram body weight serves to stop the hemorrhage quickly. Protamine counteracts heparin milligram for milligram.

Dicumarol. This substance (bis-hydroxycoumarin) was discovered in spoiled sweet clover and is the cause of certain hemorrhagic tendencies in cattle. Its cheapness represents a great advantage over heparin. Another advantage is the fact that it can be given orally. On the other hand, no satisfactory preparation for parenteral use has as yet been found. A great disadvantage is the necessity to estimate the prothrombin time daily.

Dicumarol inhibits prothrombin formation in the liver and causes a prothrombin deficiency. The prothrombin test is not simple and requires meticulous work and careful selection of the thromboplastin used. Therefore, the administration of this drug is permissible only when adequate and responsible laboratory facilities are available, and the daily dose should be given only when the result of the daily test is known. The daily amount may be given at one time and not in divided doses, since dicumarol works after a latent period of 1 to 3 days. This is, of course, a great disadvantage at the onset of treatment; it is therefore a common procedure to start with heparin and to continue with it for one or two days until the effect of the dicumarol, given simultaneously, becomes manifest.

Another disadvantage of the use of dicumarol is the occasional sudden and quite erratic unpredictable change of the prothrombin time which seems to be influenced by the intake of proteins. The values are usually said to be more stable if the patient takes 3 to 4 glasses of milk daily. Absorption of dicumarol is irregular and is increased with constipation and decreased with diarrhea. Alcohol should not be taken while dicumarol is used. No aspirin should be prescribed because salicylates have an effect similar to that of dicumarol. The hypoprothrombinemic effect of a small dose of dicumarol is much greater if congestive heart failure exists.

Contraindications to its use are similar to those of heparin, the most important being open wounds, ulcers in the gastrointestinal tract, diseases of the blood, old age, marked hypertension, hepatic disease, renal disease with disturbance of liver function, diabetes, hyperthyroidism, essential hypoprothrombinemia, poor nutrition, blood dyscrasias and subacute bacterial endocarditis. Such side effects as nausea, vomiting, or diarrhea may become so severe as to prevent their use in some patients.

The urine and stools should be watched closely and the urinary sediment examined daily for an increase in the number of red blood cells. Hemorrhage may occur in varied areas such as the nose, rectum, kidneys, stomach, eyes, and very often into the retroperitoneal tissues. This latter complication causes a rather

typical clinical picture which is often misinterpreted. The hemorrhage behind the peritoneum and the accumulation of large amounts of blood in this area may lead to sudden shock caused by the acute loss of blood or the severe pain and abnormal reflexes. If the hemorrhage takes place in the right lower abdomen, unnecessary emergency surgery may be performed for a nonexistent acute appendicitis; if located on the left side, an operation may be performed for a perforated diverticulum. Sometimes this hemorrhage leads to urinary retention. In exceptional cases who survive this event the lower abdomen and upper thigh show widespread bluish discoloration from the hemorrhagic suffusion.

Death from retroperitoneal hemorrhage seems to occur particularly in patients with peripheral arterial embolism when sympathetic block is performed while anticoagulants are being used. On the other hand, Pratt claims that this event occurs only if a large vein is torn. It must be stressed that hemorrhages do not always occur at the peak of *hypoprothrombinemia*. They may be missed with marked hypothrombinemia and may occur with relatively slight change from the normal level.

Serious bleeding is said to occur in 1 per cent of patients treated, milder hemorrhage in 6 per cent. Unfortunately, in our experience these accidents appear a little more frequently than the figures indicate.

The initial dose for an adult of 60 kilograms weight is 300 mg. given in a single dose. It is recommended to follow on the next day with 200 mg. This is often dangerous, especially in patients with myocardial infarction and shock or in hyperreactors who are not rare. We administer the second dose after 48 hours. On the following days, when the effect of this therapy on the prothrombin time becomes manifest, the dose is adjusted to the results of the prothrombin tests. Usually 25 to 100 mg. are necessary. The results of the tests are expressed in prothrombin times or in percentage of the normal. The goal is to keep the prothrombin time around double the control value of a normal individual, or between 20 and 30 per cent of normal. A normal blood sample should be tested daily in order to be sure of the activity of the thromboplastin used in the laboratory. If *the control shows prothrombin time of 14, one may say that with a prothrombin* time of the patient of 14 seconds there is 100 per cent prothrombin activity, with a prothrombin time of 22 seconds there is a 30 per cent activity, with a prothrombin time of 30 seconds the activity is 20 per cent, and it is 10 per cent with a time of 45 seconds.

When the laboratory reports a prothrombin time of 40 seconds or more, no dicumarol is given on that day. With a prothrombin time of 35 to 40 seconds, the daily dose is 25 to 50 mg. according to whether one feels the prothrombin time to be stable or still ascending. With a prothrombin time of 30 to 35 seconds the daily dose is 50 to 100 mg., and it is 100 to 150 mg. when the time is under 30 seconds.

If bleeding occurs, an intravenous infusion of 500 ml. of whole fresh blood is useful, and the administration of a vitamin K_1 preparation is advised.

Vitamin K preparations are given intravenously in doses of 70 to 100 mg If the prothrombin time remains high this injection must be repeated every 4 hours Quicker and more reliable action (Gamble et al) can be obtained by the intra venous administration of an emulsion of vitamin K_1 oxide given slowly in an amount of 5 to 10 mg of phytonadione Ten to 50 mg of K_1 orally in orange juice reduce the prothrombin time within 3 to 6 hours Vitamin K_1 is now the preferred substance If the prothrombin time reaches 60 seconds 10 mg of phytonadione should be given in orange juice even without bleeding The ambula tory patient who takes dicumarol should have tablets of 10 mg of phytonadione with him take them immediately and call his physician These substances are also the treatment of choice for the anticoagulants discussed below Following the administration of large doses of vitamin K and K_1 the patient is refractory to dicumarol for from several hours to a few days

Tromexan This is a derivative of dicumarol (ethyl biscoumacetate) and represents the first new synthetic preparation of this group to promise advantages It is more rapidly absorbed and works within 24 hours Its effect disappears usually (not invariably) faster that is within 24 hours which makes it safer when hemorrhages occur It has the disadvantage however of great lability of its effect with unpredictable rises of prothrombin time Its potency is about one fifth of dicum arol and the initial dose therefore is 1500 to 1800 mg The maintenance dose is select ed according to the prothrombin tests which must be done daily but it is usually 300 to 900 mg daily One tablet contains 300 mg and tromexan is given in divided doses several times a day Because of a rebound of the prothrombin level withdrawal of the compound should be gradual

Warfarin (Coumadin) sodium is a derivate of dicumarol that can be admin istered orally or intravenously and that produces a therapeutic level of the prothrombin time in less than 24 hours The intravenous injection acts a few hours earlier but the dosage is the same According to Clatanoff et al warfarin is comparable to tromexan in the quickness of its action The control of a stable prothrombin level seems easier

One starts with a dose of 50 to 75 mg given orally or intravenously (1 mg /Kg) The daily maintenance dose based on the prothrombin time should amount to 5 to 10 mg

Hypersensitivity is occasionally observed

In the event hemorrhage occurs vitamin K_1 is a good antidote

Marcumar (a hydroxycoumarin) is a new effective anticoagulant (Koller and Jacob Burgain et al) The dose is about 20 mg on the first day and then 3 to 5 mg daily

Phenylindanedione (phenindione) Several commercial preparations of this compound (Danilone Hedulin) are in use since Soulie employed it for the first time clinically It has dicumarol like action without being related to it Like tromexan it works quickly and is less cumulative than dicumarol The pro thrombin time returns to normal within 24 to 48 hours after therapy is discon tinued An average patient of 70 kilograms weight takes 150 to 200 mg as the

initial dose and 50 to 100 mg daily as the maintenance dose regulated by prothrombin tests Sometimes patients show a great resistance to this drug and do not respond with a change of the prothrombin time for days Jaundice and granulocytopenia have been reported (Shapiro) but in general this is a satisfactory preparation

Other Anticoagulants Synthetic heparin like preparations are available (heparinoids) They are effective and have the advantage of being much cheaper but they have one great disadvantage a severe alopecia may appear after these drugs are employed for a few weeks This phenomenon has been described in a mild form also after the use of tromexan and dicumarol but it is much more pronounced after the synthetic heparinoids Usually after a few months the hair begins to grow back

Therapy with anticoagulants in venous thrombosis should be continued for 6 to 10 days and then ambulation be permitted Because of the slow onset of action of many anticoagulants and the short duration of the treatment heparin is the therapy of choice

Cosgriff using anticoagulants observed 3 1 per cent embolisms in 96 patients with venous thrombosis none lethal Of 107 patients with pulmonary embolism the author found subsequent embolism in spite of the therapy with anticoagulants only in 2 8 per cent One patient died 10 minutes after the initial dose of heparin

Surgical Therapy

Venous ligation is rarely performed at present This is due in part to the fact that thrombi and pulmonary embolism originating proximal to the ligation was observed in about 6 per cent of postoperative patients Mostly however venous ligation was abandoned because therapy with anticoagulants was so successful Only in rare cases e g when anticoagulants are contraindicated or when no laboratory facilities exist is the operation performed

It should be done bilaterally the femoral vein just distal to the inflow from the vena profunda femoris being usually ligated Unfortunately a large percentage of postoperative pulmonary embolisms arise from the pelvic veins (prostatic plexuses) and ligation of the inferior vena cava although occasionally lifesaving is a formidable procedure

It is difficult to decide when a patient with thrombophlebitis or a proven venous thrombosis should be allowed to walk If bed rest is enforced for too long a period the danger of new thrombi becomes great Too early movement is associated with the danger of embolism Therefore some chance is always taken regardless of the decision

Treatment of Pulmonary Embolism

If a patient has just experienced an embolism of the main trunk of the pulmonary artery it is too late for therapy Embolectomy in pulmonary embolism is rarely applicable and success is even more uncommon

To relieve the anxiety and dyspnea in embolism of smaller arteries morphine should be given (0 01—0 02 Gm) If available an oxygen mask should be used There is some evidence that inhalation of 100 per cent oxygen widens the pulmonary arteries Since the greatest danger in embolism of the smaller pulmonary arteries is reflex vascular spasm every attempt should be made to prevent it For this purpose nitrites and papaverine in particular have been used The intravenous injection of 0 04—0 05 Gm of papaverine repeated in two hours if necessary seems to be a very useful procedure for the relief of vasospasm In addition atropine and ergotamine tartrate may be administered since clinical and experimental observations (Bardin) emphasize the importance of autonomic reflexes in the pathologic physiology of pulmonary embolism Preparations containing atropine ergotamine and phenobarbital (Bellergal tablets) are available and seem to be of help Three tablets daily may be used prophylactically in those patients who are apt to develop a pulmonary embolus We like spasmalgin a mixture of pantopon papaverine and belladonna

Phlebotomy has been recommended for relief of the markedly increased pressure in the lesser circuit Digitalis is not indicated unless the embolism occurs in a patient whose heart is already on the verge of decompensation or when recurrent emboli cause chronic strain and failure of the right ventricle In these cases unfortunately digitalis does not afford the customary rapid relief that otherwise occurs when this drug is indicated in cardiac patients

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Chapter 9

Irradiation of Autonomic Reflexes to and from the Heart

EARLIER REFERENCE WAS MADE to the great importance of reflexes in the causation of various types of dyspnea and of some disturbances following pulmonary embolism Reflexes will receive further consideration in the discussion of such subjects as peripheral vascular diseases and angina pectoris

It may not be amiss to review briefly other better known reflexes that occasionally influence cardiac action This subject has been neglected in text books and consequently though many of these reflexes are not rare their effects are unrecognized when encountered There has been some skepticism about the existence of such reflexes since often they cannot be elicited at will in man and their occurrence has scarcely been analyzed statistically Therefore the authors friends and colleagues who represent the basic sciences and who never see cardiac standstill when pleura or pericardium are opened and never see cardiac asystole when one of their animals swallows do not believe in such reflexes Nevertheless medical literature abounds with individual examples of their effect Fortunately most of this literature had been compiled at least up to 1937 in an excellent monograph (Schweitzer)

The discovery of pressoreceptors in the ascending aorta and in the carotid sinus and the recognition of their reflex influence on cardiac action blood pressure respiration the tonus of the urinary bladder stomach and intestines and on adrenal secretion and the formation of urine has led to more general appreciation of the fact that the activity of one organ may be influenced by autonomic reflexes from another distant organ (irradiation of autonomic reflexes) (Kisch)

Irradiation of sensory reflexes has been known for more than a century J Mueller mentioned the cold chills occasionally experienced while listening to certain classical music and the sneezing that occurs when a person leaves a dark room and is exposed to sudden light The contraction of somatic body muscles causing a chill during the contraction of the urinary bladder at the end of urination is a relatively common phenomenon in many healthy individuals and indicates an irradiation to somatic structures from an autonomically innervated organ

Disturbances of cardiac activity due to irradiation of autonomic reflexes are not rarely observed These derive largely from the fact that the activity of no other organ can be measured with the same exactitude and ease

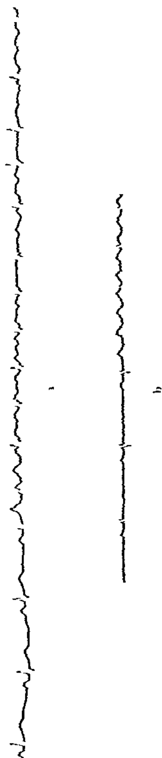


Fig 0 Deep br athing cau s atrial fibrillation (a) or flutter (b)

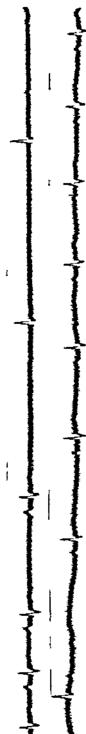


Fig 1 V luntary respiratory stan l till l ads to inhibition of the sinus n le with A V n lal escape

Just as the heart may respond to autonomic reflex stimuli it may also provoke them. The diarrhea and vomiting of coronary thrombosis and the short dry cough accompanying every extrasystole in some patients exemplify reflexes from the heart to other systems (Scherf and Schott).

Reflexes from the Respiratory System to the Heart

These reflexes have been well studied and their existence is indisputable. They were examined early by experimental method.

Instillation of chloroform, ammonium chloride and other irritating substances into a rabbit's nostril causes reflex bradycardia and cardiac arrhythmia. In dogs and rabbits arrhythmias can be elicited by mechanical irritation of a certain spot on the posterior nasal septum near the middle turbinate. Not infrequently syncope is produced in man when certain areas on the nasal mucosa are touched.

Bradycardia, cardiac standstill and arrhythmias following mechanical or chemical irritation of the larynx, the trachea and bronchi have been produced experimentally in man. This may explain sudden fatalities during operations, during bronchoscopy and after the aspiration of small particles of solid food or fluid. In one patient with glossopharyngeal neuralgia cardiac arrest with syncope occurred. Section of the ninth nerve intracranially cured the patient (Ray and Stewart).

Of great interest are the cases in which deep inspiration causes atrial extrasystoles or even atrial fibrillation. One patient (Burak and Scherf) had atrial fibrillation or flutter whenever he took one or two deep breaths. During a period of observation extending over several months attacks of atrial fibrillation could be elicited at will.

In another personal observation a 64 year old man complained of attacks of palpitation and it was discovered that transient atrial flutter and fibrillation was regularly induced by deep breathing (figure 20).

The immediate cessation of many attacks of paroxysmal tachycardia by deep inspiration or the Valsalva experiment (activation of all expiratory muscles with a closed glottis) is well known.

Of interest in this connection is figure 21 which was obtained from a 59 year old patient with coronary sclerosis, angina on effort and a sinus tachycardia. Whenever over an observation period of several weeks the patient held his breath the atrium was inhibited and deeper centers escaped. This phenomenon was observed in any phase of the respiration as long as breathing stopped. Here we are dealing in all probability not with reflexes but with an irradiation of impulses from the respiratory centers to the vagal centers.

Sudden collapse and even death during the induction of an artificial pneumothorax is often due to air embolism. When this accident happens just as the needle is inserted, reflexes may play a role and the term "pleural shock" seems justified. Mere opening of the pleura by the surgeon or ligation of a bronchus may cause cardiac asystole.

Reflexes from the Digestive System to the Heart

In 1864 Goltz reported reflex cardiac inhibition by the application of mechanical stimuli to the abdomen shortly afterward reflex disturbances of cardiac rhythm were noted during the insertion of a gastric tube in animals

A patient who had just been recovering from tonsillitis had ventricular standstill whenever an area in the pharynx near the soft palate was touched with a probe The same patient developed attacks of Stokes Adams syndrome regularly on swallowing In order to enable the patient to eat it was necessary to anesthetize the area whence the reflex was initiated (Medvei and Uiberall) A few days later the attacks disappeared completely Attacks of paroxysmal tachycardia are often terminated when the patient puts two fingers deeply into his throat to elicit retching or an emetic reflex

The occurrence of heart block and paroxysmal tachycardia during swallowing is not uncommon Atrioventricular conduction disturbances have been induced by the distention of an esophageal traction diverticulum (Weiss et al) In a patient with atrioventricular block attacks of the Morgagni Stokes Adams type appeared during straining at stool and could always be elicited by gentle digital (mechanical) stimulation of the rectum They were due to ventricular tachycardia and ventricular fibrillation (Scott and Sancetta)

The influence of irritation of various abdominal organs (liver gall bladder colon) on cardiac activity — the appearance of extrasystoles in patients with gallstones for example — is so generally appreciated that no detailed discussion is warranted The effect of gastric or esophageal distention on coronary blood flow has been the subject of investigations and marked changes are reported The coronary blood flow diminishes with distention of the stomach and lower esophagus Some patients actually complain of anginal pain when they start eating

Other Reflexes

In lower animals (crustacea) cardiac action can easily be influenced from the skin The arrest of paroxysmal tachycardia by mechanical irritation of the outer ear or pressure on the eyeballs is due to a reflex transmitted over the trigeminal nerve The reduction of coronary blood flow in dogs by the blowing of cold air on the skin has considerable clinical significance

There are other similar reflexes in which the heart does not participate Abdominal symptoms are common in the pneumonias of children and in pulmonary embolism as was mentioned earlier (Bingold) Paralytic ileus may occur in pulmonary embolism or extraperitoneal urologic operations (two personal observations) Ileus in nephrolithiasis anuria from obstruction of a single ureter by a stone (reno renal reflex) and fainting when the rectal mucosa is stimulated by an enema illustrate the irradiation of some autonomic reflexes

For the most part vagal fibers are used as pathways for these reflexes but there is convincing evidence for the participation of sympathetic fibers

Certain conditions must be present for these reflexes to appear a certain status of the receptors the reflex arc the centers and the receptive organs is necessary The importance of the status of the effector organ is shown by the fact that the same mechanism (deep breathing carotid pressure swallowing) may initiate or abolish arrhythmias

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Chapter 10

Rheumatic Fever

THE CLINICAL PICTURE OF RHEUMATIC FEVER is protean but the histologic finding are typical We are dealing with a clinical entity Despite the fact that the active disease may be unassociated with fever for a long time and may run its course without rheumatism the term rheumatic fever has been almost impervious to many attempts at replacement

INCIDENCE

Although it is a disease of major importance the exact incidence is unknown for rheumatic fever is not generally reportable in the United States and many mild cases escape recognition Possibly 500 000 to 1 000 000 people living in the United States have hearts damaged by rheumatic fever and it is estimated that rheumatic heart disease occurs in two per cent of our school children Rheumatic fever the cause of 98 per cent of heart disease in people under 20 years of age occurs most often between the ages of five and twelve It is the cause of death in almost all patients suffering from fatal heart disease between five and 24 the over all yearly death rate of this disease throughout the U S A has been between 40 000 and 60 000 The general trend both here and abroad now however seems toward a decreased incidence of the disease According to White the incidence fell from 39 5 per cent of all heart diseases in the year 1925 to 23 5 per cent in 1950 An increase in the number of instances of coronary disease and hypertensive heart disease may make this decrease more apparent than real

ETIOLOGY

Relationship to Group A Hemolytic Streptococci Although the cause of the disease is unknown some relation between rheumatic fever and infection with group A hemolytic streptococci (of which more than 40 subtypes exist) seems established Repeated infections appear necessary It is estimated that rheumatic fever follows three to five per cent of all streptococcus infections including scarlet fever The disease seems to be caused by sensitivity to antigens against protein products of certain forms of streptococci Viral infections have been repeatedly suspected but without proof Epidemics of streptococcic pharyngitis or tonsillitis have been followed in seven to 21 days by epidemics of rheumatic fever Such incidents have been observed in barracks training centers schools and camps The streptococcus infection is often subclinical An infection of the

upper respiratory tract a few days to a month prior to rheumatic fever is a common occurrence in a large number of cases Rheumatic fever may also follow an infection elsewhere e g after an appendicitis

The apparent success with which antibiotics given early during a strepto coccal infection prevent the appearance of rheumatic fever and the effect of sulfonamide and penicillin prophylaxis in preventing recurrences speak strongly in favor of streptococcal infection as an etiologic factor

The increased titer of antistreptococcic lysins and other serologic reactions obtained in the blood of patients with rheumatic fever is also suggestive of the etiologic role of streptococcic infection but it is still not conclusive evidence

Overexertion chilling trauma (Glazebrook and Thomson) and vaccination against smallpox (Freud) may lead to a recrudescence or recurrence of an attack These factors are more comprehensible in view of the work of Selye who dem onstrated that arthritis and myocardial lesions similar to those seen in rheumatic fever are found as a consequence of stress and belong to the picture of the general adaptation syndrome

Allergy At present it is widely assumed but not proven that rheumatic fever results from a chronic streptococcal infection which in some individuals causes the connective tissue to respond abnormally with exudation and prolifera tion Myocardial and coronary lesions similar or according to some identical to those of rheumatic fever can be obtained by injecting horse serum into rabbits to produce anaphylaxis or serum sickness This supports the opinion of those who regard rheumatic fever as the consequence of a hypersensitivity to bacterial products

Accordingly the pathogenesis of rheumatic fever is explained by the existence of hypersensitivity to streptococci resulting from repeated low grade infections or the persistence of foci of infection in the body Under suitable conditions when certain organisms or their products are disseminated in the tissues these tissues react abnormally producing the characteristic picture of rheumatic fever While this hypothesis as well as variants designed to embrace the hereditary and environmental conditions are not uniformly accepted allergy or some related state appears to be the most acceptable theory for the pathogenesis of rheumatic fever pending further discoveries

Heredity This seems to play a role for genetically susceptible individuals acquire the disease at an early age The appearance of several instances of rheu matic fever in a single family however has been explained by an exposure to the same infection the same nutrition and the same living conditions — in other words to environmental conditions

Social Status Rheumatic fever was once called a disease of the poor for it was believed to be associated with living in dampness overcrowding and poverty While it is more frequent in the slums it is by no means rare in higher income classes

Race Racial susceptibility has not been established

Age Rheumatic fever is primarily a disease of infancy and childhood Acute rheumatic fever has been reported in the newborn (Kissane and Koons) but in these cases the mother invariably seems to have suffered from the active disease during pregnancy Although it is not rare in children at the age of two years the peak of incidence is between five and twelve When the age of 15 years is reached 70 per cent of the patients have already been affected The acute manifestations become rare in older individuals but instances of the first attack after the age of 60 years are known An apparently first attack of acute rheumatic fever has been observed in a patient 74 years of age During the past year we have observed three instances in a hospital caring for 2000 aged patients all three cases were beyond the age of 65 but we were unable to determine whether this attack was the first

Sex There is no striking difference in incidence between the two sexes in most regions but girls seem particularly susceptible in some areas The disease tends to appear somewhat later in boys than in girls

Avitaminosis In respect to nutrition a deficiency of vitamins (A B C and even D) has been frequently asserted to favor the development of the disease Crucial evidence that vitamin deficiency has etiologic importance in rheumatic fever has not been provided The low blood levels of vitamin C frequently reported may be due to an inability to utilize the vitamin during the disease

Proteins in Diet Of interest is the statement that rheumatic fever is less common in farming areas than in places where the diet is deficient in proteins eggs in particular

Climate The role of climate in the incidence of the disease is not definitely established Rheumatic fever is more common in cold than in warm climates and is more frequently encountered in the changeable weather of the northeastern Atlantic states and of the British Isles than in Arizona Florida or California However it is frequent in dry and sunny Colorado In the New England states and the eastern section of the United States the disease is more prevalent in late winter and early spring than in summer or early autumn (Sutton) In the tropics the disease is rare except on high plateaus (Clarke) Its occurrence becomes less frequent if endangered patients are removed to subtropic climates where streptococcal infections are less common This prevails only while the patient remains there for return to cold climate often leads to reactivation

PATHOLOGY

The first change seems to appear in the mucoprotein ground substance of the collagenous tissues (Klinge) It is associated with swelling and necrosis of the latter

The *Aschoff body* is essential to the histologic diagnosis of rheumatic fever It has never been found in man in other conditions This pathognomonic lesion when fresh consists of a small focus of necrosis scattered lymphocytes and peculiar large epithelioid cells arranged in the shape of a fan This granuloma is specific for rheumatic fever although the large cells with their peculiar nucleus

alone are not characteristic In the myocardium the Aschoff body ultimately disappears leaving a scar

The interfibrillary ground substance consists of chondroitin sulfuric acid and hyaluronic acid The latter is depolymerized by an enzyme hyaluronidase The relation of this enzyme to rheumatic fever has been widely discussed of late but is not clear A certain spreading factor which increases tissue permeability has been discovered in testicular extracts and group A hemolytic streptococci This factor was recognized as hyaluronidase and this substance is antigenic The amount of antihyaluronidase is greater in patients with rheumatic fever Salicylates are reported to inhibit the spreading reaction of hyaluronidase and the antirheumatic effects of this drug have been attributed to this action Crucial evidence has not yet been submitted

Rheumatic fever is a disease of the mesenchyme and involves connective tissue everywhere However the responses in different organs vary Thus typical Aschoff bodies are not found in the lungs although perivascular infiltrations and alveolar exudation appear they are also absent from the brain

Vascular System Inflammatory reactions are often discovered at the root of the pulmonary artery and aorta Similar changes occur regularly in the systemic arteries in the peripheral vessels of the lungs and especially in the coronary arteries They consist of round cell infiltrations changes in the intima media and adventitia with hyaline exudate which obstructs the small vessels A glomerulitis is demonstrable in over 20 per cent of the cases

Joints and Serous Surfaces The same changes are noted in the joints and in some serous surfaces such as the pleura and pericardium In these tissues the exudate is predominately serous The joint cavity may be distended by fluid exudate which contains fibrin and a few granulocytes The synovia is edematous and hyperemic The periarticular tissues are involved in a similar manner and Aschoff bodies may persist in these structures for a long time

Heart In the heart myocardial involvement with the formation of Aschoff bodies seems to occur in 100 per cent of the cases (Talalaeff) This holds at least for all cases of fatal rheumatic fever Myocardial changes are also caused by the vascular alterations mentioned above by degeneration of the myocardial fibers diffuse myocarditis and infiltration with eosinophilic leukocytes

In a large percentage of cases changes appear in the endocardium along the line of closure of the valves This happens particularly on the atrial surface of the mitral and tricuspid valves and on the ventricular surface of the aortic valves Here also swelling of the fibers and of the ground substance secondary necrosis of the fibrilli and migration of granulocytes and fibroblasts are the primary changes Secondary deposits composed principally of fibrin produce small warty vegetations verrucous endocarditis At the beginning the verrucae can easily be removed but invading capillaries and fortifying connective tissue gradually attach them more securely to the valve Verrucae also appear on the chordae tendineae and on the endothelium of the chambers The mural endocardium of the posterior wall of the left atrium is often affected Healing leads to

thickening of the endocardium and valves to retraction stiffening and fusion of the cusps and valves and to shrinkage and fusion of the chordae tendineae with eventual secondary degeneration and calcification Frequently the pericardium is also involved (pancarditis) Involvement of the valve rings and ascending aorta as well as pulmonary artery occurs and facilitates later enlargement of these structures if failure and congestion develop

The pericardial changes are described in a later chapter Marked alterations are also found in the diaphragm

Lungs Apart from ordinary bronchopneumonia other pulmonary complications may appear which are characterized clinically by fever severe cough and bloody sputum dyspnea occurs in these patients In this rheumatic pneumonia an alveolitis is found with buds of connective tissue filling and obstructing the alveolar ducts They have been called bourgeons conjonctifs or Masson bodies and they are said to represent the characteristic pulmonary equivalent of the Aschoff body in rheumatic fever The specificity of the Masson bodies has been recently denied (Herbert and Manges) Atelectasis is common Physical findings may be scarce X ray studies show massive density or radiation of opaque shadows from the hilus into the lung fields The arteries of the lung especially in the smaller divisions may show an obstructive arteriolitis Acute fibrinous or serofibrinous pleurisy also occurs with or without pneumonitis

Subcutaneous Tissue The firm rounded subcutaneous nodules are gray and translucent They are composed principally of edematous connective tissue and cellular infiltrations lacking definite arrangement The presence of Aschoff bodies in these nodules is exceedingly rare

Nervous System Proliferative arteriolitis with occlusion of small vessels and focal malacia of the central nervous system especially of the cortical gray matter and meninges have been described repeatedly The pathologic picture often resembles a meningo encephalitis but the spinal fluid usually remains normal These changes are mentioned to explain the acute and even chronic psychoses such as schizophrenia which may follow rheumatic fever Epileptiform convulsions are said to be seven times as common in patients who have had rheumatic fever as in the general population (Foster)

Atherosclerosis Atherosclerosis especially coronary sclerosis is often considered a final stage of the arterial involvement in rheumatic fever It seems however that rheumatic fever does not predispose to coronary sclerosis Experience shows that the incidence of coronary atherosclerosis is no higher in rheumatic fever patients than in nonrheumatics despite the fact that the coronary artery lesions described above are demonstrable in approximately one half the patients dying of an acute attack of rheumatic fever

SYMPTOMS

Insidious Onset Often the onset is very insidious so that the disease is easily overlooked Accordingly the number of patients is rather large (30 to 40 per cent) who at a later date develop complaints from a valvular lesion due to an earlier

but entirely unrecognized rheumatic fever This feature and the fact that cardiac changes are not invariably permanent make the compilation of accurate statistics exceedingly difficult

General Symptoms In many cases loss of appetite profuse sweating loss of weight irritability fatigue restlessness slow growth abdominal pain and lassitude as well as anemia are the first and sometimes the only manifestations of the disease Epistaxis is common Since salicylates have an anticoagulant action some authors attribute the epistaxis to the administration of large doses of salicylates Epistaxis often occurs however in acute rheumatic fever before any medication has been given

So called growing pains are common manifestations of a synovitis localized in the region on the hamstring tendons behind the knee but they may have other causes which are not related to rheumatic fever In the latter instance they are usually felt in the muscles and tendons rather than in the joints They are rare in the upper extremities and do not cause pain on motion

Local Symptoms The clinical picture of an acute migratory arthritis with inflammation redness extreme tenderness and swelling of the joints successive involvement of one joint after another and the tendency to involve the large (knee elbow) as well as the small joints (bones of the hands feet spine jaw) is well known This syndrome of acute polyarthritis is more common in childhood and becomes infrequent with increasing age The arthritis may be monoarticular and need not migrate Return of normal joint function within a short time is the rule

At other times the disease may begin abruptly with vomiting acute abdominal pain and tenderness in the right lower quadrant This may suggest acute appendicitis (pseudosurgical cases) The abdominal pain has been explained by the presence of an arteritis in abdominal organs as well as by a rheumatic mesenteric lymphadenitis These abdominal signs respond well to salicylates Cardiac symptoms symptoms indicating pulmonary pathology or involvement of the nervous system may dominate the clinical picture

Pain over the precordium or retrosternal pain is very common and in most cases is due to involvement of the coronary vessels it may become aggravated if acute pericarditis develops

The widespread involvement of small arteries in active rheumatic fever accounts for the protean picture

SIGNS

Fever Fever is often absent If present it may persist for days or months While it may develop into a hyperpyrexia of 111 degrees F this is rare Temperatures of 103 degrees F are common There is profuse sweating

Joints An important sign suggestive of the correct diagnosis is redness and swelling of the joints with periarticular inflammation causing pain which is sometimes extremely severe This statement is particularly valid when the original joint involvement subsides in approximately eight days while other

joints are successively invaded in the interim In classical cases the arthritis is associated with general malaise pallor anorexia and weight loss Cold clammy sweats and profound prostration are also present In these cases the diagnosis is simple In the absence of joint involvement however diagnosis by physical examination alone may be exceedingly difficult

Skin Erythema multiforme is common Erythema marginatum (circinatum annulare) with pale centered ringlets over the flexor surface of the joint is considered pathognomonic Erythema nodosum and purpuric eruptions also occur as unspecific reactions

Subcutaneous Tissue The occurrence of subcutaneous rheumatic nodules is considered frequent in some countries and relatively uncommon in others Such nodules are infrequent in adults They are reported in approximately 1 to 4 per cent of the American cases but the latter figure presumably includes more juvenile cases Since the nodules are painless the search for them must be conducted with patience in the areas usually affected the extensor surface in the neighborhood of the elbows wrists and knees and over flat bones as in the scalp They are often symmetrical They appear in crops and may persist for weeks When large they are readily detected but small ones require careful palpation because the non tender masses may be no larger than peas Later the nodules become firmer fibrous and more circumscribed These rheumatic manifestations which disappear as healing occurs are important because they constitute a sign of activity Some consider them a sign of a more virulent process

Lungs Pneumonitis is not uncommon Some authors found it in 11 per cent of the cases It begins with fever dyspnea cough and pleural pain and imitates the picture of atypical pneumonia It seems particularly common in children and may lead to a fulminating clinical picture and death Rales and dullness are found Roentgenograms show bilateral symmetrical multilobular infiltrations often simulating pulmonary edema (Seldin et al) Pleurisy with effusion is common

Heart Since cardiac involvement is exceedingly common and acute myocarditis seems to be invariably present during the active phase examination of the heart may aid in the diagnosis Moreover repeated careful observation of the heart is necessary especially in early childhood for many of these patients succumb to cardiac complications during the active phase

A sinus tachycardia is present and the heart rate may reach 140 per minute The cardiac rhythm is usually regular since the respiratory arrhythmia otherwise so common in the healthy heart particularly during childhood tends to disappear In some cases arrhythmias due to conduction disturbances (periodic dropped beats or Wenckebach s periods) develop Extrasystoles and atrial fibrillation are rare

Palpation reveals a hyperactive heart as in hyperthyroidism This hypermotility is also demonstrable fluoroscopically and in the absence of other diseases (hyperthyroidism anemia cardiac neurosis) is considered a valuable sign of active rheumatic carditis The heart may be enlarged This always indicates severe

myocardial damage an ominous development if it occurs early in the active phase Cardiac dilatation is frequently seen in ambulatory patients in whom marked myocardial damage existed and in whom the diagnosis was overlooked for some time Occasionally this dilatation disappears rather quickly as the patient recovers from the acute phase In many cases the enlargement of the cardiac shadow is more apparent than real since it is due to the formation of a pericardial effusion

At times the heart sounds are impure distant and split Since splitting or duplication of the heart sounds is a common event in normal people particularly in childhood this does not necessarily mean cardiac involvement but sudden appearance of this sign is important A presystolic gallop occurs if conduction time is prolonged With more severe myocardial damage the sounds are muffled and a diastolic type of gallop rhythm is heard The differentiation of this type of gallop rhythm from the physiologic third heart sound which is common in children may be impossible (see chapter on myocardial diseases)

Systolic murmurs over the apex and the pulmonic area are heard frequently Changes in the valvular ring with consequent relative mitral insufficiency and edema of the valves are offered as an explanation of the former while a rheumatic mesopulmonitis with dilatation of the supravalvular portion of the pulmonary artery and formation of eddies is held responsible for the latter Probably the cardiac hypermotility tachycardia and the fever contribute to the appearance of systolic murmurs These early systolic murmurs do not indicate valvular involvement for it requires many months before the connective tissue can shrink sufficiently to produce actual valvular changes

In 75 per cent of the cases these systolic murmurs disappear within six months In many patients with acute rheumatic fever no lasting disturbance of cardiac function remains The longer and more severe an attack the more probable is involvement of the valves At the termination of the first attack of rheumatic fever Ash found no evidence of heart disease in 59 2 per cent of the patients

Diastolic murmurs have been described repeatedly in the acute phase They are transient and are explained perhaps by the rapid diastolic influx of blood into the dilated ventricles Often impure sounds and diastolic accidental sounds are confused with murmurs indicative of structural damage A pericardial friction rub is audible in a large percentage of the childhood cases when the search is repeated sufficiently often and with great diligence Effusions are common

Laboratory Tests The white blood cell count the sedimentation rate the electrocardiogram and other tests are important and may help establish the diagnosis and aid in estimating the progress and in detecting recurrences The findings are not characteristic of rheumatic fever but they yield invaluable information in conjunction with other clinical data

Leukocytosis is common the total figure may exceed 20 000 A count above 9000 is considered by some indicative of an active process With relapse the white blood cell count rises sometimes before other evidence of the recurrence is demonstrable Persistent leukocytosis often but not invariably speaks in favor of con

tinued activity A normal leukocyte count however does not preclude an active process

Usually a progressive anemia due to bone marrow depression develops rapidly early in the active phase

Urine Marked sweating occasionally results in a drastic reduction of the urinary output The specific gravity of the urine rises and the color is dark Often the highly acid urine deposits urates on cooling Albuminuria is not uncommon in the febrile cases and red blood cells may be found in the sediment The latter findings are important and should be checked frequently sometimes hematuria has been reported to be the result of salicylate therapy Acute nephritis occurs but its relationship to rheumatic fever is not clear

Erythrocytic Sedimentation Rate This test or Weltman s coagulation test has primary importance in determining the degree of activity of the process Figures of 100 to 130 (Westergren method) are not rare in the active stages of the disease *Sometimes tachycardia and increased sedimentation rate are the sole* indications of persistent activity at other times only the latter is found But exceptions that is activity in spite of a normal sedimentation rate are not rare This became clear when the appendices of the left atrium were resected during commissurotomy in patients with mitral stenosis Histologic examination revealed Aschoff bodies in 30 per cent of the specimens examined despite absence of clinical evidence of activity According to some authors these Aschoff bodies represent a healed stage (Tedeschi et al) When pulmonary congestion supervenes the rate of red blood cell sedimentation is lowered

Streptococcal hemolysins dissolve red blood cells Antibodies are formed which are called antistreptolysins Individuals who have recently had a streptococcal infection form an antibody which neutralizes the O (oxygen labile) hemolysin of certain beta hemolytic streptococci The titers in rheumatic fever are high in 85 per cent of the cases in the active phase But similar titers (250 and above) *are seen for a long time following any streptococcal infection The test is not* specific and does not indicate progress of the lesion

C reactive protein Apparently this is one of the most valuable tests During various infections or necrotizing processes a protein appears in the blood which reacts differently from any other blood protein with the C polysaccharide of pneumococci in vitro It is a precipitation reaction This antibody is developed by hemolytic streptococci A precipitate is formed with a test reagent consisting of antiserum prepared in rabbits by immunization with purified C reactive protein However the test may be negative despite activity of the process On the other hand it is not reversed by congestive heart failure as is the sedimentation rate It is suppressed by salicylates cortisone and ACTH and is absent in normal blood There is thus no normal range Any positive reaction is abnormal

MUCOPROTEINS Estimation of the concentration of mucoproteins in the serum has been said to be a useful index of rheumatic activity The test is nonspecific The mean value for healthy children is 2 5 mg percent In rheumatic children values of 8 5 mg per cent are found

OXALACETIC TRANSAMINASE In active rheumatic fever the serum concentration of the enzyme glutamic oxalacetic transaminase is increased (Nydick et al)

Electrocardiogram This is altered in most instances of active rheumatic fever if tracings are registered sufficiently often changes are found in 95 per cent of the cases The changes may come and go within a few hours — *ten negative* tracings may be followed by a positive one Frequent registration of the electrocardiogram in active rheumatic fever has served to reveal the high incidence of myocardial involvement and the peculiar affinity of this disease for the specific tissue of the heart Prolongation of the P R interval is the most common finding The normal P R interval should not exceed 0 16 second in infants 0 18 second in childhood and 0 21 second in the adult In rheumatic fever the values often exceed 0 21 second Occasionally higher degrees of block or even complete heart block appear These changes are usually transitory Some maintain that prolonged atrioventricular conduction time is due to increased vagal tonus or to an increased response of the heart muscle to vagal stimuli since the prolongation is abolished by atropine This conclusion seems unwarranted in view of the fact that the normal conduction time is also markedly shortened by this drug In rare cases the P P interval remains permanently prolonged after full recovery of the patient

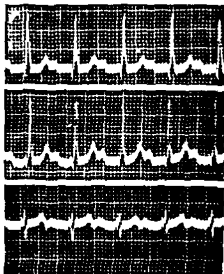


FIG 22 Sinus tachycardia and prolonged atrioventricular conduction time (0 26 second) in a patient with active rheumatic fever

Figure 22 shows an electrocardiogram obtained from a 12 year old boy with active rheumatic fever The atrioventricular conduction time is prolonged to about 0 24 second There is a tachycardia of 124 beats per minute since P is hidden in the T the exact measurement of the beginning of the P wave is impossible *Abnormal T waves and evidence of intraventricular block especially right* bundle branch block often occur

CLINICAL COURSE

The manifestations and duration of the active phase of rheumatic fever varies In the past overemphasis has been laid on the joint manifestations often they are absent Mono and polycyclic forms have been described the first being about twice as common as the second In the monocyclic type only *one series* of joints is affected in rapid succession whereas in the polycyclic type there are repeated exacerbations with and without joint manifestations over a long

period of time There is also a continuous form which persists for several years

The elevated sedimentation rate increased leukocyte count and other evidence show that the period of activity frequently lasts for years although much of its evolution is subclinical At other times notably in early childhood the stormy signs of activity may be fulminating and the manifestations are alarming Within a few weeks either the severe myocardial damage causes congestive heart failure which does not respond to treatment or else a pericarditis develops In many of these cases death cannot be prevented Sometimes the initial picture is rather severe but the subsequent recovery proceeds without leaving much trace of damage as far as the clinical examination reveals

In general the course of rheumatic fever is unpredictable and variable but the cases can be grouped readily into three categories

(1) Cases in which the process dies out entirely leaving the patient without cardiac damage or with a minimal injury compatible with a long and active life

(2) Cases in which the patients develop a valvular lesion following the first or second attack of rheumatic fever which persists compensated for a variable time often throughout a long and active life

(3) Cases in which the process is active for many years with frequent relapses increasing disability and death at an early age

All possible variants of these three groups may be found

Fortunately hyperpyretic rheumatic fever is rare In this variety temperatures of 43 degrees C and higher occur and the cerebral centers regulating temperature are presumed to be affected perhaps as a part of an encephalitis These patients usually have delirium a symptom otherwise uncommon as long as rheumatic fever is uncomplicated and the patient has not received large doses of salicylates Skin eruptions are frequently present most of the patients succumb

Recurrences of rheumatic fever are common especially in children but are less frequent after the age of 14 years Many patients in the childhood group who recover from rheumatic fever suffer from a recurrence within one year The average risk for a major recurrence of rheumatic fever is 25 per cent in patients who are four to 13 years old and 8 6 per cent in patients between 14 and 16 The risk of a major recurrence is many times greater in the year following a period *of active rheumatic fever than in subsequent years (Wilson and Lubschez) It is* often difficult to decide whether we are dealing with a recurrence or a recrudescence of an existing attack These observations have an important bearing on prophylactic measures especially in endangered children

For reasons already mentioned and particularly because so many cases of rheumatic fever escape diagnosis it is difficult to ascertain the incidence of permanent cardiac disease If obervations are limited to people known to have had active rheumatic fever residual cardiac disease may be expected in 85 per cent Others as mentioned above place the incidence at 50 per cent or less but all agree that the percentage rises with subsequent attacks Another factor in statistical variation is the duration of the follow up often the time elapsing after the acute phase is too short for a positive statement In a four to eight year

follow up study of veterans Engleman Hollister and Kolb found rheumatic heart disease as a sequel to rheumatic fever in 23 7 per cent of 135 men In a study of 1000 patients with rheumatic fever Bland and Duckett Jones found evidence of rheumatic heart disease in 44 per cent at the end of an observation period of 20 years

Signs of Activity These are fever joint inflammation increased sedimentation rate positive C reactive protein leukocytosis temporary changes in the electrocardiogram tachycardia and the presence of subcutaneous nodules Only one or two of these signs need be present

DIFFERENTIAL DIAGNOSIS

Occasionally this is very difficult Earlier when discussing the gastrointestinal symptoms of rheumatic fever we alluded to a possible confusion with appendicitis

The differentiation between rheumatic pneumonia and pulmonary congestion is likewise often difficult while stiffness of the neck or delirium may simulate meningitis The pulmonary manifestations may lead to the diagnosis of bronchopneumonia or pleurisy and the renal changes with subsequent hematuria and cylindruria may suggest the erroneous diagnosis of acute nephritis Confusion with poliomyelitis is said to be common

Great care must be exercised to exclude an arthritis of gonococcic origin Not rarely the latter may be polyarticular whereas rheumatic arthritis may be limited to a single joint so that the opportunity for error is great The rapid relief afforded by adequate doses of salicylates in rheumatic fever may help in the differential diagnosis of this type of arthritis

Very difficult is the differentiation between rheumatic fever and the syndrome following infection with streptococci Joint pains and cardiac changes appear in both conditions This question is discussed in the chapter on myocarditis The wrong diagnosis of influenza is often based on noncharacteristic complaints and fever

There are several acute infectious diseases which may be associated with a secondary polyarthritis The related features of scarlet fever dysentery and so forth usually make the differential diagnosis relatively easy Likewise the circumstances under which a septic arthritis with great joint destruction develops usually precludes diagnostic errors Unfortunately this is not always the case in an acute osteomyelitis Osteomyelitis has a more intense local symptomatology and the process is at the epiphysis rather than in the joint moreover the constitutional reaction is severe Nevertheless childhood osteomyelitis is often considered rheumatic fever until sepsis develops the mistake may be fatal Rheumatic fever may also be confused with undulant fever and miliary tuberculosis (Freud et al)

According to the modified criteria of Jones for the diagnosis of rheumatic fever the presence of two major criteria or one major and two minor criteria indicate a high probability of the presence of rheumatic fever

Major criteria are (1) carditis (as manifested by the presence of significant murmurs increasing cardiac enlargement as seen by x ray examination pericarditis congestive heart failure in the absence of other causes) (2) polyarthritis (3) chorea (4) subcutaneous nodules and finally (5) erythema marginatum

Minor diagnostic criteria are fever arthralgia prolonged P R interval in the electrocardiogram increased sedimentation rate presence of C reactive protein and leukocytosis and evidence of preceding infection with beta hemolytic streptococci The presence of a previous history of rheumatic fever or of inactive rheumatic heart disease are also minor diagnostic criteria

Sickling Disease In sickling disease the appearance of dyspnea arthritis cardiac enlargement with a prominent conus of the pulmonary artery the presence of systolic and even diastolic murmurs and changes in the electrocardiogram may cause confusion Anemia and thrombotic occlusion of small pulmonary and coronary arteries seem responsible for many of these findings The presence of lymphadenopathy jaundice anemia reticulocytosis no response to salicylates and a normal sedimentation rate speak in favor of sickling disease The possibility that in rare instances rheumatic fever and sickling disease may coexist (Plachta and Speer) should be borne in mind

Rheumatoid Arthritis In adults active rheumatic fever often resembles rheumatoid arthritis since the latter disorder may start in abruptly with all features of rheumatic fever Subcutaneous nodules occur in 15 to 20 per cent Sometimes distinction is possible only after prolonged observation since the initial picture is the same as in rheumatic fever Formerly narrowing of the joint spaces and limitation of motion as well as poor response to salicylates were considered suggestive of rheumatoid arthritis In recent years cardiac manifestations such as electrocardiographic changes the appearance of valvular lesions and the like have been reported in rheumatoid arthritis Among 25 cases of infectious arthritis 14 showed evidence of cardiac involvement identical with that found in rheumatic heart lesions (Baggenstoss and Rosenberg) Even structures resembling Aschoff bodies and subcutaneous nodules have been reported There is much support for the opinion that both conditions are variants of the same pathologic process (Klinge) The occurrence of cardiac manifestations in such patients however is more rare in our experience than is indicated by some authors On the basis of their experience with 100 patients with rheumatoid arthritis and 13 post mortem examinations Egelius et al denied that the incidence of myocarditis or endocarditis is increased

PROGNOSIS

Many patients succumb in or shortly after the active phase of this highly serious disease while a large number die in the prime of life from its consequences

Generally speaking the prognosis is more serious when the initial manifestations are severe when activity persists for a long time or when the disease begins early in life Only 69 per cent survive childhood and only 35 per cent live through adolescence when the process starts early Fifty per cent of the patients

die within nine years of the onset and only five per cent live beyond the age of 45 (Cohn and Lingg) The more pronounced the myocardial damage is and the earlier cardiac failure develops the worse the prognosis If a permanent valvular lesion develops the prognosis depends mainly upon such recurrences and complications as atrial fibrillation or pulmonary embolism Nevertheless it is not uncommon to see a patient who developed a rheumatic valvular lesion at the age of five or six years and is still active and well at 70 or 75

A good deal depends upon the treatment during the attack and thereafter In this respect the great advance made in recent years justifies the hope for remarkable improvement in the prognosis in the near future

CHOREA

Sydenham s chorea is related to rheumatic fever but the precise association is obscure It is a childhood and adolescent disease and is more common in girls whereas as mentioned earlier rheumatic fever affects both sexes equally Sulkiness and emotional outbursts are early signs

Many physicians regard chorea simply as another manifestation of rheumatic fever In 20 per cent of cases of chorea rheumatic heart disease develops although there has been no other evidence of rheumatism (Sutton and Dodge) According to other studies the incidence of heart disease in cases of pure Sydenham chorea is over 50 per cent Some observers believe chorea is succeeded by cardiac complications only when there has been other evidence of rheumatic infection It is even asserted (Usher) that valvular disease is never the consequence of chorea per se but rather that it is due to an intercurrent rheumatic infection In one patient with signs of chorea but no other evidence of active rheumatic fever however death occurred accidentally and an active rheumatic endocarditis was found at necropsy (Sutton and Dodge)

While leukocytosis and fever may be absent in chorea it is possible that these signs of activity have vanished by the time chorea appears The sedimentation rate in chorea is normal

Of 134 patients with chorea without any other manifestation of rheumatic fever only 3 per cent developed heart disease (Jones and Bland) The authors consider chorea to be a mild manifestation of rheumatic fever not particularly conducive to the development of rheumatic heart disease

Pheumatic endarteritis of the cerebral vessels (meningoencephalitis) with perivascular infiltrations has been observed and pronounced changes may be found in the corpus striatum

TREATMENT OF PHEUMATIC FEVER

A distinction should be made between the treatment of the active phase of rheumatic fever and the measures designed to prevent a recurrence

Bed Rest This is necessary in active rheumatic fever and must be enforced as long as signs of activity persist and at least three weeks after the sedimentation

rate returns to normal Increased heart rate fever and progressive electrocardiographic changes are also indications for rest Bed rest need not be absolute in a majority of cases — the patient may have bathroom privileges

Prolonged rest is extremely important for despite the acuteness of some of its manifestations rheumatic fever is a chronic disease The process may be active and progressive even in the absence of symptoms of poor health

In the acute stage with arthritis some thought should be given to the proper type of bed as well as to suitable clothing in view of the severe sweating attention *to these details will add greatly to the patient's comfort The situation is much* the same as in tuberculosis a disease comparable to rheumatic fever in many respects Since it is impossible to predict the duration of activity of the disease rest should be enforced for three weeks after all evidence of activity has vanished

Drugs The therapeutic agent of choice for the management of acute rheumatic arthritis is sodium salicylate which has been employed for more than half a century in this disease Many observers believe that the drug furnishes such prompt relief that this in itself may provide a therapeutic diagnosis While there are patients who do not respond those whose joint pains are not caused by rheumatic fever may obtain relief from salicylates It seems that sodium salicylate does not influence the course or duration of the disease nor the progress of complications but it is capable of rapidly dissipating the joint swelling relieving pain and acting as an antipyretic Large doses of sodium salicylate at regular intervals are recommended A typical daily dose might be one grain per Kg body weight or 10 grains every 4 hours It has been claimed that when large amounts of salicylates are given day and night a favorable effect is exerted on the course of the disease and cardiac complications can be prevented This is denied by others There is no doubt that the doses of sodium salicylate which were formerly administered were often too small Large doses are more beneficial It has been claimed that the quick relief of inflammation and pain in the joints is due to the fact that salicylates stimulate protein catabolism and alter the water content of the cells (Reid et al)

Intravenous administration has been repeatedly recommended in order that a high therapeutic blood level be reached To be sure it is not always easy to maintain or even reach a high blood level without such untoward effects as tinnitus deafness diarrhea headache nausea or vomiting Occasionally these complaints disappear despite continuation of treatment Dizziness mental confusion and disturbances of vision or breathing (Kussmaul s respiration) may appear Since larger doses are employed more often instances of salicylate poisoning are being reported more frequently in medical literature (Troll and Menten)

Hypoprothrombinemia is observed during the administration of large doses of salicylates particularly if more than six grams are given daily If hemorrhage occurs preparations of vitamin K should be given

Salicylates are said to inhibit the spreading effect of hyaluronidase Like aminopyrine they affect enzyme reactions

The combination of salicylates with sodium bicarbonate for oral administration may diminish gastric irritation This has been said to prevent the attaining of a high salicylate level in the plasma However this finding has not been confirmed Other salicylate preparations and magnesium carbonate in place of sodium bicarbonate have been recommended but these compounds have not been tried on a sufficiently wide scale to form a sound judgment

Sodium salicylate can be replaced by acetylsalicylic acid (aspirin) the dose of both compounds is identical To avoid side effects others recommend an aspirin dosage ¾ of the dose of salicylates and double the amount of sodium bicarbonate Sodium is to be avoided in heart failure It is important to administer these compounds every four hours day and night in the amount of 0 15 Gm per kilogram in twenty four hours This dose is reduced if deafness tinnitus or nausea appear In the case of nausea and vomiting sodium salicylate can be given rectally in an amount of 4 to 5 grams in 150 ml of warm starch water Stolzer recommends 60 mg of aspirin per pound body weight for two days then 40 mg /lb for the third to seventh day and 30 mg /lb from the eighth day on Instead of sodium salicylate one may administer sodium gentisate which is a metabolic product of the former The dosage is identical

Because of the appearance of the rebound phenomenon this treatment is not discontinued suddenly doses are gradually diminished when all signs of activity have disappeared The shortened sedimentation rate during therapy with salicylates (or ACTH or cortisone) is not always a sign of improvement but is accounted for by the inhibition of production of fibrinogen and globulin in the liver

Rarely patients either are refractory to salicylate therapy or display untoward symptoms even when relatively small amounts are administered For these cases aminopyrin (Pyramidon) has been repeatedly recommended Doses of 2 to 5 grams daily have been given over long periods without the development of toxic symptoms This treatment carries with it the risk of agranulocytosis If frequent determinations of the white blood cell count are carried out to detect the early onset of this rare complication no danger is involved Untoward accidents are more common during the administration of cincophen derivatives which are rarely used in acute rheumatic fever

The administration of sulfonamides *in the treatment of active* rheumatic fever is abandoned Penicillin is given in the amount of 600 000 units daily in the beginning for one week in order to eradicate infections with streptococci Then one injection of bicillin is given monthly (see below) No particular success has been observed from the administration of antistreptococcic sera and vaccines In patients sensitive to penicillin one of the broad spectrum antibiotics is indicated

ACTH AND CORTISONE The administration of pituitary adrenocorticotropic hormone (ACTH) and of adrenocortical hormone (cortisone) in patients with rheumatic fever in the active stage has a profound influence on the process Within 1 to 2 days the fever subsides the toxemia disappears arthralgia is relieved the sedimentation rate slowly becomes normal a pericardial effusion

is absorbed tachycardia disappears and even the rheumatic nodules vanish in a few weeks These effects however are rarely lasting and discontinuation of the administration of these compounds in most cases is soon followed by reappearance of activity

As with the administration of salicylates here al o the discussion continues on whether the illness is actually shortened by these compounds or whether complications are prevented It seems that this may be the case if treatment is started very early although the same has been claimed — without proof — for salicylates as well

There is no doubt that in certain cases these hormones may be lifesaving This is especially true in juvenile patients with advanced cardiac failure that does not respond at all to standard therapy Here the admini tration of corti one or ACTH may lead in the first few days to an aggravation of the condition because of sodium and water retention Nevertheless marked improvement soon takes place Even if cessation of therapy leads to the reappearance of signs of congestive heart failure this can be relieved by the same compounds indeed it is often possible to carry the patient over a critical period in this manner Pretreatment with cortisone before mitral surgery diminishes the incidence of histologic signs of activity

Cortisone has the advantage of being active even if given orally but ACTH has a more prolonged effect Two tablets of cortisone acetate of 25 mg are given four times daily or 120 units of ACTH are injected daily (3 injections of 40 units each) In some patients this therapy is tolerated for six to eight weeks For prolonged treatment the daily dose of cortisone in men should not exceed 50 mg and in women 30—40 mg

According to Stolzer cortisone is given intramuscularly in a dose of 300 mg on the first day 200 mg daily on the second to fifth days and 100 mg daily up to the thirty fifth day and 75 mg daily from the thirty sixth to forty second day Smaller doses are needed when the newer stronger similar compounds are given

In children one starts with 80 units of ACTH on the first day followed by 60 units on the second and 40 units daily after two or three days

Another recommended dosage for corticotropin intramuscularly is as follows on the first to fourth day 120 units daily 100 units daily from the fifth to seventh days 80 units daily from the eighth to fourteenth 60 units daily from the fifteenth to twenty first day and then 40 units daily to the thirty fifth day and 20 units daily until the forty second day

Prednisone (Meticorten) is given in the amount of 75 mg daily in divided do es every 8 hours The therapy is continued for 4 weeks in the same dosage then about 5 mg less daily The total duration of the therapy should last if possible 8 to 12 weeks

The patient should be watched carefully for side effects Among others the e are rounding of the face (moonface) with acne and Cushing s syndrome (striae hypertension hyperglycemia and glycosuria sodium and water retention)

hirsutism distention of the abdomen mental depression and psychoses The patient should be kept on a sodium poor diet (less than 500 mg of sodium daily) diuretics should be given and potassium ions in the form of fruit juice or 1 to 3 grams of potassium chloride by mouth daily Occasionally an old tuberculosis becomes activated The compounds in particular cortisone and related compounds (hydrocortisone Meticorten) should not be discontinued abruptly The dose is reduced gradually to avoid rebound effects with fever thrombophlebitis rheumatoid arthritis and pleurisy

Recent comparative studies revealed no superiority of treatment of rheumatic fever with these hormones as compared to salicylates Phenylbutazone cortisone corticotropin sodium salicylate and paraaminobenzoic acid are of equal value so that patient s tolerance for the treatment is of decisive value (Kalliomaki) The question is still open It is possible that further studies will show that early therapy with adequate dosage administered for a sufficient time does prevent cardiac involvement and shortens the illness Less rebound phenomena are observed if cortisone is combined with paraaminobenzoic acid and salicylates Some observers suspect that the modus operandi of salicylates is also via the adrenals

Symptomatic Cardiac Therapy Occasionally it is necessary to treat cardiac complaints and complications symptomatically Although digitalis is administered when the patient shows evidence of passive congestion or cardiac failure it often fails to produce the desired response since the myocardial damage is too far advanced Paracentesis may be necessary for large pericardial effusions At times morphine must be given for a short period to control pain Codeine may be advisable to relieve the cough

Diet During the early period fluids should be administered freely and the diet should be light After the first week high caloric but easily digestible diet is indicated Various vitamins have been recommended although the value is uncertain Large doses of ascorbic acid (100 to 200 milligrams daily) are often recommended There is no proof of a beneficial action of succinic or benzoic acid or for the inhalation of oxygen which has been advocated Treatment of the anemia can be postponed until early convalescence Any of the usual iron preparations (ferrous salts) will suffice

Chorea There is no specific treatment for chorea Bed rest quiet surroundings and sedation may afford relief The use of some arsenical preparation such as Fowler s solution is a time honored procedure While some physicians have failed to observe any good effects from ACTH or cortisone others seem to have employed the drugs with success

After Care Even after signs of activity have vanished patients must be watched carefully for a recurrence The young patient especially is susceptible to a new attack after a cold or a sore throat In general children should not return to school for several months after an attack so that they may be protected against new infections and overexertion Plans should be made for the child to receive instruction after convalescence is well under way It may be difficult

to convince parents of the necessity of prolonged care but emphasis upon the fact that cardiac damage may progress as long as there is any sign of active rheumatic fever helps them to understand the importance of a well ordered prolonged recovery phase

Education It is important to educate parents and teachers about rheumatic fever and its subclinical stages (anorexia loss of weight) in order to aid in the early recognition of reactivation or recurrence

Local Treatment Apart from general therapy there remains the perennial question of local treatment of the joints The use of cradles to lift bed clothing from the affected extremities and fixation of painful joints by splints and similar measures deserve consideration since they add to the comfort The value of heat local application of methyl salicylates and similar agents counter irritation and the like is disputed but sometimes they make the situation more tolerable Sponge baths with a weal alcohol solution should be used daily In very rare cases with extreme distention of a joint and the resultant pain the problem of aspiration of the exudate in the joint may come under consideration Aspiration should be done only with complete surgical asepsis It should be emphasized that this is rarely necessary

PROPHYLAXIS

Recurrences are common and each attack means more damage to the heart Preventive therapy often neglected in the past is therefore of great importance

Tonsillectomy One of the oldest measures to prevent a recurrence is tonsillectomy for tonsillitis often precedes the first and subsequent attacks However the success of this operation is not impressive it has been reported that the number of recurrences is not influenced at all by the operation This limited success might be anticipated since pharyngitis like any other infection with hemolytic streptococcus *may precipitate active rheumatic fever* The operation is justified however in patients with recurrent tonsillitis or evident infection of the tonsils Naturally the operation should never be performed during active rheumatic fever and it should not be done too soon after an acute bout of tonsillitis At least 6 to 8 weeks should elapse between the disappearance of acute tonsillitis and operation A bacteremia following tonsillectomy has been found in 28 per cent of the cases Penicillin should be given (600 000 units) daily for five days pre and postoperatively

Environmental Changes The proposal to isolate children and to prevent contact with others in the same age group (sanatoria or convalescent homes with careful selection of their children) has several advantages but obviously is limited in practical application Another method to prevent recurrences is to have the endangered patient move away from possible sources of infection that is crowded areas Permanent transfer to southern climates is also to be considered but the hardship involved in dislocating families and the expense of moving plus the fact that rheumatic fever does occur in the tropics makes such a procedure difficult

Streptococcal Throat Infections

It is estimated that more than 3 per cent of all patients who have a throat infection caused by hemolytic streptococci develop rheumatic fever It is now known that penicillin therapy instituted very early will markedly reduce the incidence of rheumatic fever even though it fails to prevent it in every instance consequently all streptococcal infections particularly those in children should be treated with antibiotics According to Weinstein in patients with scarlet fever who are treated early with only 15 000 units of penicillin intramuscularly every 3 hours for 10 days rheumatic fever appeared in 7 per cent

According to the recommendation of the American Heart Association in children it is best to give 300 000 units of procaine penicillin with aluminum monostearate intramuscularly and to repeat the injection again after three and six days In adults 600 000 units of procaine penicillin in oil are injected intra muscularly every third day

For oral therapy children may take tablets of 200 000 adults 300 000 units one hour before each meal and at bedtime i e four times a day Treatment should be continued for 10 days

If the patient is sensitive to penicillin erythromycin can be given 10 milli grams per pound in four divided doses daily for two days and one half this amount daily for the next eight days

Prophylaxis Therapy carried out throughout the year is indicated in all patients who have had rheumatic fever or chorea particularly if a valvular lesion developed One should start soon after the diagnosis of rheumatic fever is made

Penicillin is given twice daily orally in the form of a tablet containing 200 000 units before breakfast and preferably an hour before meals The injection of 1 200 000 units of benzathine penicillin G (bicillin) once a month is highly recommended but allergy or local pain often prevent this therapy Lozenges or troches of penicillin should not be employed Sulfadiazine in the amount of 1 gram may be given every morning but this should not be employed if the patient has any evidence of allergy Gantrisin is also effective Rashes sore throats and leukopenia necessitate immediate interruption of this form of therapy

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Chapter 11

Bacterial Endocarditis

Bacterial endocarditis may be divided into acute and subacute forms but the distinction is often arbitrary Patients whose illness does not last over six to eight weeks are assigned to the acute type In this form the picture is invariably that of sepsis In the subacute variety septic phases may appear but weeks or even months may elapse before evidence of more than slight infection and bacteremic stages are encountered The introduction of penicillin changed these clinical syndromes and early treatment cures most cases of the acute and subacute type quickly There is however a much more potent reason for separating the acute and subacute forms acute bacterial endocarditis usually involves healthy hearts as a complication of general sepsis while subacute bacterial endocarditis (or endarteritis) is a disease involving abnormal hearts or vessels Actually the duration of both acute and subacute bacterial endocarditis may be the same and another term for these conditions would seem desirable

Acute Bacterial Endocarditis

Etiology This lesion also called malignant or ulcerative endocarditis is an infection caused by highly virulent microorganisms It may accompany any type of sepsis pneumonia osteomyelitis puerperal fever or sinus thrombosis The causative agents are hemolytic streptococci staphylococcus albus and aureus pneumococci gonococci and influenza bacilli Sometimes the colon bacillus or the meningococcus is found Among 44 cases of acute bacterial endocarditis hemolytic streptococci were found in 21 staphylococcus aureus in 11 bacterium coli communis in 5 and gonococci in 2 Two other patients had meningococcus infections one staphylococcus albus and two a mixed infection (Phipps) The bacteremia is not always demonstrable

Pathology Sometimes the valvular vegetations are small and are arranged like those of rheumatic endocarditis more often they are large and irregularly arranged The favorite sites of development are the atrial aspect of the mitral and tricuspid valves or the ventricular side of the aortic valves The large thrombi are composed of clumps of bacteria between layers of fibrin and leukocytes The vegetations may appear on a normal valve or on one previously diseased If multiple the vegetations may attain a diameter exceeding 1 cm and in this instance they may render the orifice stenotic The firmly attached vegetations usually have a friable lobulated surface With necrosis of the valvular tissue an

ulcer forms with a shaggy base covered by a clot If the ulceration penetrates a leaflet aneurysm or perforation may follow

Symptoms Signs The clinical picture can hardly be separated from that of sepsis Irregular chills sweating high widely fluctuating fever extreme malaise headache and anorexia prevail in the symptomatology Very often the participation of the heart in the process is not discernible for the cardiac manifestations (tachycardia and a systolic murmur) stand in the background in comparison to the signs of sepsis Owing to the stormy course of the disease there is rarely time for the formation of valvular alterations capable of producing diastolic murmurs The latter alone would establish cardiac involvement The spleen is often enlarged and sometimes tender Sooner or later petechiae appear in the skin or conjunctiva The white blood cell count may be increased to 30 000 The urine shows albumin and red blood cells Not infrequently embolic occlusion of a large vessel in the spleen kidneys brain mesentery or extremities rapidly changes the picture

Acute bacterial gonococcic endocarditis in previous years was not rare One author found it in 26 per cent of all his patients with acute and subacute bacterial endocarditis in the preantibiotic era Acute nephritis and uremia are frequent complications Pneumococcic endocarditis which often involves the valves of the right heart was rapidly fatal The pulmonic valves occasionally are affected in other forms of bacterial endocarditis

The progressive anemia leukocytosis the course of the disease and its complications are the same as those of sepsis

Prognosis In the past the disease usually has been fatal and cases with evidence of healing were only rarely encountered Instances of healing even of gonococcal endocarditis have been reported but these were rare as indicated At the present time with the general use of antibiotics most patients including those who suffer from septicemia caused by meningococci or staphylococci are saved Therapeutic problems however do arise when the agent (staphylococci) does not respond readily to the antibiotics or when the illness is recognized too late

*Therapy Penicillin is the antibiotic of choice in most cases With meningo*coccal sepsis sulfonamides are more useful The other antibiotics are used according to specific indications (see below)

SUBACUTE BACTERIAL ENDOCARDITIS

Subacute bacterial endocarditis (endocarditis lenta) has been separated from acute bacterial endocarditis chiefly by virtue of its prolonged course and certain features resulting from this time factor and the nature of the etiologic agent The patient developing subacute bacterial endocarditis already has an acquired or congenital cardiac abnormality After World War II an increased incidence of this disease was observed in countries where widespread malnutrition was rampant

Etiology and Pathogenesis The causative agent in over 90 per cent of the cases is streptococcus viridans which is an organism of low virulence This group of streptococci can be subdivided into several strains Of special importance is the most common causative agent the streptococcus salivarius which responds readily to penicillin treatment another streptococcus fecalis (enterococcus) is a normal inhabitant of the human intestines In rare cases hemolytic streptococci meningococci influenza bacilli staphylococcus aureus and albus diplococcus pneumoniae Escherichia coli Salmonella Neisseria catarrhalis streptobacillus moniliformis Bacillus proteus Pseudomonas aeruginosa and even gonococci — all agents usually responsible for the acute type of bacterial endocarditis — may produce the subacute form when the virulence of the provocative agent is low In rare cases streptothrix candida albicans and members of the Brucella group are etiologic factors Occasionally two or even three microorganisms have been found simultaneously

Under normal conditions blood plasma and leukocytes destroy the streptococcus viridans quickly even when large numbers are injected intravenously fibrin however which is soon deposited on affected endothelium and endocardium protects the microorganism from destruction Blood is bacteriocidal only for organisms free in the circulation In subacute bacterial endocarditis the body seems biologically immune to the infectious agents in contrast to the hypersensitive reactions of the connective tissue to hemolytic streptococci in rheumatic fever

PREVIOUS CARDIAC CONDITIONS It is very unusual for a subacute bacterial endocarditis to develop in a healthy heart Even if the valves occasionally seem normal on gross examination histologic sections usually reveal new or old rheumatic changes In a vast majority of cases an old rheumatic valvular lesion is present In this respect the mitral valve is involved a little more commonly than the aortic valve Not rarely subacute bacterial infection is superimposed upon a congenital heart lesion especially on a patent ductus arteriosus a ventricular septum defect or coarctation of the aorta In rare cases the disease develops on the basis of a syphilitic aortitis or atheromatosis

The cardiac malformations which form the basis for subacute bacterial endocarditis sometimes are too trifling to produce any clinical symptoms or signs Thus the disease may develop in patients with bicuspid aortic valves of a congenital type (bicuspid valves are occasionally the result of a former rheumatic infection) or on a malformed pulmonic valve

Of interest is the discovery of subacute bacterial endocarditis in the dog as the result of strain Mural and valvular vegetations were observed after the creation of a large arteriovenous fistula in dogs and were also seen clinically in this condition (Lillehei Parmley et al) presumably because of the combination of stress and infection Subacute bacterial endocarditis was found in a patient with mitral regurgitation caused by rupture of a papillary muscle which resulted from myocardial infarction (Leman) in mural thrombi following myocardial infarction (Joffe and Feil) and after endocardial trauma in connection with

cardiac catheterization Bacterial endocarditis may appear during treatment with ACTH owing to diminished resistance In arteriovenous fistulas the focus spreading the infection was occasionally the fistula itself and the patients were cured by its extirpation

Evidence of active rheumatic fever is found in an astonishingly high percentage of patients with subacute bacterial endocarditis Some pathologists have found activity (presence of Aschoff bodies) in most of their patients with rheumatic heart disease who succumbed to subacute bacterial endocarditis The streptococcus viridans infection is often implanted on a fresh rheumatic valvulitis The disease seems to follow various infections which erode the endothelium and produce deposits of fibrin

Trauma and contamination suffice Streptococci of the viridans type are often present in the blood one wonders as Sir Thomas Lewis did why subacute bacterial endocarditis does not occur more frequently

An experimental form of the disease can easily be provoked by creating a valvular lesion and injecting streptococcus viridans into the blood stream The mechanical factor in its appearance is demonstrated by the fact that the lesion develops on that part of the valve which is most exposed to mechanical irritations In a patent ductus arteriosus the lesion occurs in the wall of the pulmonary artery where the blood forced by aortic pressure through the duct strikes the wall of the artery in a patent ventricular septum the lesion develops in the right ventricle at the point where blood is forced through the septal defect and in coarctation of the aorta it is found near the stenotic isthmus In the cases of patent ductus arteriosus and aortic coarctation we are of course dealing with an endarteritis rather than an endocarditis

PORTAL OF ENTRY The most frequent portal of entry is the upper respiratory tract after which comes the urogenital system otitis and wound infections Not rarely subacute bacterial endocarditis follows a perfectly normal delivery

There is a frequent opportunity for implantation of streptococci in areas with damaged endothelium since blood cultures often reveal the presence of streptococcus viridans in patients without subacute bacterial endocarditis In rheumatic fever nonhemolytic streptococci are found in almost 10 per cent (Lichtman and Gross Swift and Kinsella) Streptococcus viridans bacteremia is common after irritation of foci of infection — after massage of infected gums or tonsils for example Among 138 patients who had teeth extracted a transitory bacteremia due to nonhemolytic streptococci was found in 60 9 per cent the incidence was even higher (75 per cent) in patients with a chronic mouth infection Among 110 patients with a septic mouth streptococcic bacteremia was found in 10 9 per cent in a single examination irrespective of any operative procedure (Okell and Elliott) In another study (Palmer and Kempf) one or two teeth were extracted in 82 patients and streptococcus viridans bacteremia followed in 13 4 per cent The clinical experience that subacute bacterial endocarditis frequently follows extraction of teeth upper respiratory tract infections tonsillectomy and puerperal infections is in accord with these results Nonhemolytic streptococci are likewise

found in the blood after a curettage or after a simple surgical operation such as an appendectomy. Bacterial endocarditis may follow genito urinary manipulations (Beattie) or cardiac surgery (Kouwai and Nahas). From all data now available it seems that infection of the blood stream is a common event and gives opportunity for streptococci to invade a locus minoris resistentiae in the heart. Staphylococci are often found in the blood of patients who suffer from osteomyelitis and in drug addicts who give themselves injections of morphine or heroin without the necessary precautions.

AGE. The disease is observed at all ages having been reported in infants as well as in patients over 80 years old. It is not common in children however.

Incidence. It is difficult to evaluate the incidence of the disease. Apparently subacute bacterial endocarditis complicates about 5 per cent of rheumatic heart lesions. In two Boston hospitals Gelfman found subacute bacterial endocarditis in 25 per cent of patients with rheumatic heart disease. This figure does not reflect the true incidence of the disease. In congenital heart lesions it is much higher.

Pathology. Ulcers and thrombotic vegetations form on the affected valve, on the endocardium or in an artery. The vegetations consist of remnants of blood platelets, white and red blood cells, microorganisms and great masses of fibrin and vary in size, color and consistency. They may be small and nodular or they may form large irregular club shaped friable masses. The pedunculated formations are often firm and contain fibrous tissue or calcium deposits as evidence of a tendency to heal.

The vegetations may be large enough to obstruct the flow of blood. Valves may be perforated and chordae tendineae may rupture. At times mycotic aneurysms occur in various vessels but they are especially prone to develop in the aorta, the arteries of the brain and the heart, and in the extremities. Presumably they are the result of infected emboli lodging in the vessel wall. Embolism may occur anywhere and not rarely causes death. If the right heart is involved (in patients with ventricular septal defects) pulmonary embolism is frequent. Embolic or diffuse hemorrhagic nephritis is common. Acute myocarditis with hemorrhages and minute infarcts also occurs regularly (Saphir).

In all stages there may be bacteria free periods with negative blood cultures and, according to some observers, no organisms in the vegetations.

Symptoms. In many cases the disease begins insidiously with very vague and indefinite initial symptoms such as general malaise, cough, loss of weight, transitory arthralgia, fatigue, loss of appetite, sweating, aches and pains in various parts of the body. At times the onset is associated with a cold or a sore throat. Under these circumstances the physician may not be consulted until much later; months may elapse before the situation is regarded more seriously. In other cases the disease begins as a polyarthritis and resembles rheumatic fever clinically; only gradually does the picture of subacute bacterial endocarditis become evident. A sudden chill, hemiplegia or pain in the finger tips and toes caused by small emboli are the factors that impel some patients to summon a

physician and seek help Often intolerable abdominal pain indicates embolism of the spleen kidney or intestine

In many cases patients are free from complaints and are even euphoric If the fever were not present I would be well is a commonly heard statement

Signs While there is no characteristic single sign of subacute bacterial endocarditis the syndrome is so typical that the fully developed disease is easily recognized At the beginning the diagnosis is difficult and errors are committed in two directions Not rarely the unwarranted diagnosis is made on the basis of fever and a heart murmur in patients who are later discovered to be suffering from pyelitis or some other febrile disease Errors are also made in failing to consider the possibility of subacute bacterial endocarditis from the start a mistake the patient s family rarely forgives

The temperature may show all variations from a slight elevation to a septic intermittent or remittent curve with chills The fever may disappear completely for weeks and even for months

The heart rate is usually not abnormally rapid Arrhythmias are uncommon for subacute bacterial endocarditis usually develops in a compensated heart without evidence of congestion Myocardial inflammatory lesions are often present and decompensation which may occur in the course of the disease necessitates the use of digitalis

Inspection usually shows a yellow muddy (cafe au lait) discoloration of the pallid skin coincidental with a secondary anemia This secondary anemia may become a very prominent feature as the disease progresses The fingers are often clubbed Few diseases manifest such rapid development of this change Since this sign is very rare in uncomplicated rheumatic valvular disease the presence of clubbing in a febrile cardiac patient should immediately arouse the suspicion of subacute bacterial endocarditis

In a majority of cases cardiac examination reveals the typical features of a rheumatic or congenital heart lesion Occasionally the cardiac involvement is too slight to produce signs detectable by auscultation or percussion but such cases are rare Murmurs change in intensity new murmurs appear or murmurs which were present for years vanish This is because large vegetations may obstruct an orifice close a deficiency in the interventricular septum or close a patent ductus arteriosus

Petechiae often appearing in crops develop in the neck under the nails above and below the clavicle around the inner malleolus and on the conjunctiva and the soft palate They result from hemorrhage caused by small bacterial emboli in capillaries Often they have a white center due to a minute necrosis created by the embolus Splinter hemorrhages under the nails with or without this white center are not pathognomonic for they may occur in various infections and are not rare in generalized lupus erythematosus

Osler nodes are very tender pea size nodules which appear in the finger tips toes (often under the nails) and on the vola manus and planta pedis They cause local swelling and their tenderness may distress the patient for several days

According to most observers the nodes as well as the petechiae derive from emboli Others attribute them to a proliferative arteritis The skin over the affected area appears red or a redness shimmers through from the deeper parts The pain disappears in a few days and only a purple spot remains for a while The picture is modified if deeper or more superficial arteries are involved Janeway lesions are maculae or papulae not painful 1 to 4 mm in diameter appearing on the palms or the soles of the feet

Purpura occurs rarely

The spleen is enlarged and hard in about 55 per cent of the cases The enlargement is greatly accentuated by embolisms to this organ If embolism occurs late the spleen may not be palpable for several months

Laboratory tests Laboratory examination reveals a positive blood culture in 75 to 90 per cent of the cases Since as pointed out earlier nonhemolytic streptococci are not rarely found in the blood in other conditions such as rheumatic fever rheumatoid arthritis and dental infections three or four positive blood cultures should be secured if possible to verify the diagnosis On the other hand one or more negative reports do not eliminate the possibility of subacute bacterial endocarditis for the disease may be associated with negative blood cultures over a considerable period of time The incidence of negative blood cultures is reduced by the taking of fairly large amounts of blood for culture At least 20 ml of blood *should be drawn and on the first day a culture should be taken every hour for five* hours One should always employ both plates and broth cultures The best time to withdraw the blood is when the patient s temperature is rising or during a chill It is reported that the incidence of positive blood cultures is higher from bone marrow aspirations Instances are known however in which cultures were negative from the bone marrow and positive from venous blood Arterial blood has no advantage over venous blood The growth of some nonhemolytic streptococci may not be visible before three weeks

From 140 patients with nontreated subacute bacterial endocarditis Griffith and Levinson obtained 129 positive cultures on the first day of hospitalization 8 positive ones on the second day and only 3 on the third day In this connection it is important to note that less than 3 per cent of the patients who failed to show a positive blood culture on the first two days showed one later The culture is often sterile in subacute bacterial endocarditis within the right heart

In 46 per cent of 135 blood cultures Loewe and Alture Werber found a streptococcus with a distinctive combination of properties which the authors called streptococcus s b e It was the causative organism in 40 of 68 subjects with subacute bacterial endocarditis Standard dosage of penicillin often is not sufficient in these patients and the disease recurs

In every instance an anaerobic culture should be made Penicillinase should be used whenever the patient has received penicillin about 24 hours prior to withdrawal of the blood

Sensitivity tests measuring the inhibition of growth of the responsible agent by different antibiotics should be done if possible More than 90 per cent of all

strains of streptococcus viridans are inhibited by 0 01 to 0 1 units of penicillin per cubic centimeter

Usually there is a moderate increase of sedimentation rate A hypochromic anemia is common and often is progressive The white blood cell count does not change characteristically but a polymorphonuclear leukocytosis may be present However leukopenia can also occur Large phagocytic cells are occasionally seen in the blood smear The Wasserman reaction may be positive in the absence of syphilis

Electrocardiogram The electrocardiogram affords no diagnostic help Changes may appear and are to be expected in view of the frequent alterations of the myocardium but they are not characteristic Extrasystoles and atrial fibrillation are rare

Urine The urine shows a great number of red blood cells in many cases and even gross hematuria The latter may temporarily increase after renal infarction In the intervals between renal infarctions albumin hyaline and granular casts are observed

Duration This varies greatly since the course may be suddenly interrupted by a lethal cerebral embolus or the disease may assume a very protracted character and last for more than two years When the patient succumbs to a complication early in the course the diagnosis is often missed Long bacteria free intermissions with relative well being are also encountered

Complications Most of the complications are due to emboli or to mycotic embolic aneurysms The damage caused by emboli depends upon the location and size of the occluded artery and the frequency with which embolism recurs Their appearance cannot be predicted or prevented Cerebral emboli may cause hemiplegia or paresis Renal embolism is responsible for severe backache and hematuria embolism of a coronary artery may produce myocardial infarction with prolonged anginal pain as seen in coronary thrombosis Valvular thrombi cause obstruction and valvular ulcerations cause perforations Perforation of the heart may follow an abscess of the ventricular wall If the endocardial thrombi are situated in the right ventricle (as happens in an interventricular septal defect) pulmonary emboli are released and simulate the picture of a pneumonia Generally embolism causes a rise of temperature leukocytosis and increase of the sedimentation rate It should be emphasized that an embolism may occur months after the illness seems to be under control as the result of antibiotic therapy

Pericarditis occurs occasionally A subarachnoid hemorrhage may be the first sign of the disease Emboli in a peripheral artery may cause gangrene A splenic abscess may follow embolism of this organ and may rupture into the peritoneal cavity causing peritonitis

Mesenteric infarction and intestinal gangrene are occasionally observed

Uremia due to nephritis terminates the scene in a large percentage of cases The nephritis may be diffuse acute or subacute Lohlein s embolic nephritis may exist

Sometimes psychoses appear that may be connected with anatomic changes in the nervous system There is also severe headache double vision and meningeal signs caused by embolisms signs of brain abscess occur Subarachnoid hemorrhages occur because of rupture of mycotic aneurysms

Differential Diagnosis Any unexplained fever particularly in a cardiac patient whatever the age speaks in favor of subacute bacterial endocarditis The differentiation from rheumatic fever is especially difficult since both may be present simultaneously and the diagnosis of subacute bacterial endocarditis is often missed in these cases because the physician fails to consider its presence One of the most common conditions wrongly diagnosed is grippe or viral infection

Prognosis The outlook in this disease became brighter with the advent of intensive antibiotic therapy

In rare cases spontaneous recovery is possible Distinct healing processes with scar formation and even lime salt deposits have been observed at necropsy According to some estimates these spontaneous recoveries occur in 1 to 3 per cent of all diagnosed cases The latter figure is in our opinion too optimistic at least if the fully developed cases alone are taken into consideration But cases with a mild infection that run a benign course do occur they are more prone to spontaneous cure and respond better to treatment They occur more often among the cases with congenital abnormalities One must be cautious in pronouncing a patient cured for remissions may last as long as six months The prognosis is undoubtedly better for these cases where combined penicillin therapy and surgical intervention are applicable as in patent ductus arteriosus or an infected arterio venous fistula

The incidence of cures approaches 80 per cent if all cases of subacute bacterial endocarditis are considered but in bacteremia with staphylococci it drops to 52 per cent Patients die from complications such as emboli and cardiac failure even after the endocarditis is cured

Therapy Therapy starts with prophylaxis Oral sepsis must be treated carefully infected teeth and tonsils should be removed

In view of the frequent occurrence of temporary bacteremia after dental extractions or tonsillectomy antibiotics are administered prophylactically for a few days before and after tooth extraction The same method is employed for five days after delivery

The treatment of subacute bacterial endocarditis should start as soon as the diagnosis is made One should not wait for weeks until a positive blood culture is obtained since irreparable damage may be inflicted in the interim by the myocarditis or embolism It is better occasionally to treat a patient without absolute proof of the diagnosis than to wait too long

When the diagnosis is suspected five blood cultures should be taken at hourly intervals and therapy should be started immediately after It should be remembered that persistently negative cultures are not rare

The recent findings that penicillin penetrates fibrin and that it persists in tissue fluids much longer than in the blood (as well as the general availability of this antibiotic) make it the remedy of choice.

In 95 per cent of the cases the administration of 2 000 000 units of penicillin daily for a few weeks is sufficient to cure the patient. In some cases smaller doses suffice but one can never predict this in advance. If sensitivity tests are available early, one chooses a dose which is 4 to 5 times higher than that required to inhibit the causative agent in vitro. Sometimes sensitivity may be high in vitro but not in vivo. Most nonhemolytic streptococci are sensitive to 0.1 unit of penicillin per cc or less. Enterococci may be sensitive to 1 to 5 units. Experience with the sulfonamides has shown that pure inhibition does not suffice to cure the disease.

We recommend starting with the administration of 600 000 units of procaine penicillin G three times a day. Others recommend the administration of penicillin G 500 000 U every three hours. If cardiac failure is present, the potassium salt is preferred. This makes greater peak levels than repository penicillin and fibrin deposits are penetrated better. It is important to note (Eagle et al.) that if the concentration of penicillin in the blood exceeds a certain level the effect is no greater than at a lower level. In the intervals between injections when the level of penicillin falls, the bacteria do not multiply and many damaged microorganisms are disposed of by the body.

In most cases the fever subsides in a few days, an unusual sense of well being is experienced by the patient, the appetite improves, and the heart rate becomes slower. When all signs of activity disappear we continue the same dose for three more weeks. Cultures, if positive at the beginning, are taken repeatedly, even if the fever subsides; a positive culture may indicate that the dose is insufficient. One should bear in mind that fever may be due to the presence of active rheumatic fever, the absorption of abnormal diseased foci, to embolism, or sensitivity to penicillin. In the latter case another penicillin is used (penicillin O instead of penicillin G) which is antigenically different.

If there is no clinical evidence that the disease is becoming arrested or if the culture persists positive, the dose is increased. Daily doses up to 100 million units have been found necessary and have been given with success.

If enterococci are found, one starts with 10 to 20 million units daily and adds twice daily an intramuscular injection of 1 gram of a mixture of streptomycin and dihydrostreptomycin. In these cases penicillin is also administered intravenously in doses of 500 000 units or more every two hours. If the microorganism is susceptible, the dose may soon be reduced. The combination of penicillin with other antibiotics has been claimed to reduce the activity of penicillin, but this does not hold for streptomycin. In staphylococcic endocarditis a combination of penicillin with erythromycin (3 to 4 grams daily, intravenously) or bacitracin may prove successful. Sometimes bacitracin alone cures the endocarditis provoked by gram positive bacteria; 100 000 units are given daily, one third or one fourth of this amount in each dose, intramuscularly. Nephrotoxic effects have been reported.

Terramycin and Chloromycetin given alone seem merely to exert bacteriostatic effects In some instances successes have followed the use of dihydrostreptomycin combined with Terramycin Neomycin sulfate intramuscularly may help in staphylococcic endocarditis there is danger of injuring the acoustic nerve but this risk must be taken in a disease which is so serious The danger is not great if only one gram (of neomycin) is given daily for 10 days Usually 0 25 Gm is injected every 6 hours In infections with proteus or pseudomonas aeruginosa one must administer polymixin B in spite of potential renal damage This danger has been lessened by newer preparations One administers 100—200 mg daily intramuscularly divided into four doses These compounds are often lifesaving In the endocarditis of brucellosis the combination of Aureomycin with dihydro streptomycin has proved useful infections with bacillus influenzae and para influenzae may be treated with the same mixture or with Terramycin in place of Aureomycin Laboratory sensitivity tests are decisive for the choice of the antibiotic

It is of interest that 65 per cent of the patients who died when the endo carditis seemed controlled had viable microorganisms in the valves Therefore in advanced long standing disease it is well to continue therapy for more than three weeks after clinical improvement is established

For the first three or four weeks the patient must rest in bed but in the last few weeks he may be up and about provided no exertion is undertaken The circulation must be watched since myocardial damage often leads to heart failure

In order to increase the blood level of penicillin by preventing its rapid excretion by the renal tubules simultaneous administration of other agents has been recommended Caronamide seems effective 1 5 to 2 0 Gm are given every four hours Benemid diotrast paraminohippuric acid have also been employed Benamide (Probenecid Baker and Pilkington) is usually well tolerated and preferred One half gram is given every 6 hours In most cases these drugs can be omitted

After the illness seems cured the patient is advised to watch his temperature every two hours one day a week for a year so that therapy is started early if the disease shows evidence of recurrence Such recurrences are not rare Often it is difficult to decide whether a recrudescence or reinfection has occurred

Short term therapy in various forms has been recommended In one investi gation 600 000 units of aquous penicillin was given every 6 hours with a mixture of 1 0 Gm of equal parts of streptomycin and dihydrostreptomycin (Combistrep or Distrycin) intramuscularly (If not more than 2 grams of the mixture are given daily for not longer than 4 weeks vestibular damage (streptomycin) and auditory nerve damage (dihydrostreptomycin) occurs rarely) This was continued for five days the injections were then given at 12 hour intervals (Hall et al) In a certain percentage of cases this short term therapy is sufficient the type in which success will be secured cannot be foretold Therefore prolonged therapy with moderate dosage seems better than short term method

TERMINAL (CACHECTIC) ENDOCARDITIS

The small valvular vegetations in rheumatic endocarditis should not be confused with similarly located small thrombi seen occasionally along the closure line of the mitral and aortic valves in cachectic patients suffering from cancer uremia leukemia and other wasting diseases

These thrombi may reach the size of a pea and in rare instances are even larger They do not contain much fibrin but are composed mainly of amorphous masses derived from blood platelets The finer mechanism of their formation is unknown They are nonbacterial but may be invaded by microorganisms just before death

Careful histologic examination of valves showing this type of endocarditis may disclose evidence of an old rheumatic infection occasionally terminal endocarditis is superimposed on an atherosclerotic process of the valve

Patients showing this type of endocarditis not rarely have thrombosis of the systemic veins (Grant) they may even present the clinical picture of migratory phlebitis

The process is not always terminal Healing is possible if the patient recovers from the associated chronic cachectic disease Because there is no evidence of inflammation the term degenerative verrucal endocardosis has been proposed (Allen and Sirota)

ENDOCARDITIS IN GENERALIZED LUPUS ERYTHEMATOSUS

Etiology The etiology of this interesting lesion known for many years only as a skin affection is obscure It seems to be allergic in origin and belongs to the group of so called collagen diseases Sunlight may aggravate the process The resemblance to other forms of lupus is rather remote Over 80 per cent of the cases are encountered in women before the menopause although no endocrine factor has been demonstrated

Of great importance is the finding of L E (lupus erythematosus) cells that is large polymorphonuclear cells containing nuclear debris in the blood and bone marrow in rare cases they are also found in the pericardial fluid They result from the phagocytosis of free nuclear material from another leukocyte of the same type The cells are found in 96 per cent of the cases A negative test does not militate against the diagnosis False positive tests are exceedingly rare

Pathology The collagenous fibers all over the body are affected and degenerative necrotic lesions appear in the kidney skin and heart

The endocardium is involved in about 30 per cent of the cases (Libman and Sacks) Verrucae appear on both sides of the valve but not at the line of closure and mural vegetations often develop on the atrial endocardium Vegetations may also develop between the papillary muscles particularly in the right heart These changes were originally described as atypical or indeterminate endocarditis There is evidence of myocardial degeneration with interstitial infiltration and exudate *The pericardium and pleura are often involved in a fibrinoserous inflammation* Bronchopneumonia is common In the kidney a peculiar thickening of the capillary walls called wire loop changes is characteristic The skin lesions

are not pathognomonic on microscopic examination and consist of a cellular infiltration into the corium The vascular lesions are composed of capillary dilatation proliferation of the endothelium and necrotizing inflammation sometimes with thrombosis of the smaller arteries No Aschoff bodies are found and no bacteria are demonstrable in the tissues

Symptoms Signs The disease often begins insidiously with low irregular fever joint pain weakness and loss of weight A lymphadenopathy is often found Typical leukopenia is usually associated with progressive anemia and thrombocytopenia Albuminuria is common Often there is a skin eruption consisting of disc like patches with raised red edges and depressed centers When the covering desquamates dull white scars are left behind These lesions may be seen on the hands feet ears or chest in their most typical form they merge to form a butterfly pattern over the nose and on the cheeks The cutaneous signs may be outstanding but in some cases they are absent They may appear after sunburn or the use of ultraviolet light or x rays The electrocardiogram may show abnormal T waves in many or all leads

False positive serologic tests for syphilis are obtained

Physical examination of the heart shows nothing characteristic A systolic murmur may be audible and is without significance Evidence of pleural or pericardial involvement may be obtained

Therapy Cortisone (150 to 200 mg) daily or ACTH (50 to 150 mg) often arrest the illness and in a crisis may bring about improvement in 24 to 48 hours While some observers claim this improvement does not increase life expectancy others believe that the patient may be kept alive for an indefinite period (Soffer et al) After improvement the dose is reduced sometimes doses as small as 5 milligrams of ACTH daily suffice All the precautions necessary in connection with this therapy must be observed

Recently prednisone and prednisolone which are said to be four times as potent as cortisone are used in lupus erythematosus As the initial suppressive daily dose Bollet et al recommend 20 to 60 mg usually 30 or 40 mg daily as a maintenance dose 18 mg were given daily Effectiveness and limitation of therapy with these drugs are the same as with cortisone and corticotropin

RARE TYPES OF ENDOCARDITIS

Tuberculosis may cause an endocarditis in which tubercle bacilli are demonstrable in the valvular vegetations (Davie) This endocarditis in not unusual in miliary and disseminated tuberculosis and it does not affect the closure line of the valves (Baker)

A variety of organisms have been recovered from the valves including Brucella abortus and organisms such as actinomyces other fungi are also known to produce a mycotic endocarditi

In exceptional cases other agents e g erysipelothrix the causative agent of swine erysipelas causes endocarditis in man Loeffler described in endocarditis parietalis fibroplastica with eosinophilia (up to 70 per cent) in the blood

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Chapter 12

Valvular Lesions

Insufficiency of the Aortic Valves

Incidence

Insufficiency of the aortic valves, commonly but somewhat incorrectly called aortic insufficiency or aortic incompetence, is one of the most frequent isolated valvular lesions. It is most prevalent in males. The rheumatic type is usually combined with an aortic stenosis and often also with a mitral stenosis of the same origin. In recent years the incidence of syphilitic aortic insufficiency has been greatly reduced.

Etiology

Rheumatic Fever and Syphilis. The high incidence of the lesion is readily appreciated because both rheumatic fever and syphilis are responsible for deformities of the aortic valves which render them incapable of proper closure and permit diastolic regurgitation of blood into the left ventricle. The valves become thickened, deformed and retracted. In syphilis the widening of the commissures in addition to shortening of the valve aids in the production of incompetency.

Atherosclerosis. Formerly, aortic insufficiency due to atherosclerotic changes in the valve was a very common diagnosis. This was due to the fact that a syphilitic aortic insufficiency was usually mistaken for an atherosclerotic lesion. This error is partly explained by the secondary atherosclerotic changes prone to occur in fully developed syphilitic aortitis. Although aortitis has been known as a pathologic lesion for several decades, its prevalence has been noticed rather slowly by the clinician and pathologist. Very often the atherosclerotic process is so pronounced that on gross examination it conceals the underlying syphilitic aortitis, making the correct diagnosis possible only in microscopic sections.

Since no history of rheumatic fever can be elicited in an appreciable percentage of rheumatic patients, and a syphilitic infection is often denied either from ignorance or embarrassment, atherosclerotic insufficiency is diagnosed when secondary calcification has taken place in a valve altered by syphilis.

Primary atherosclerotic changes of the aortic and mitral valves are, however, so common that they may even be called physiologic. Small yellow spots appear on the aortic side of the aortic valves and on the ventricular surface of the mitral valves, that is, in places most exposed to pressure; this is seen even in patients under ten years of age. These spots represent deposits of cholesterol. They often

disappear in children but recur and later persist Still later the amount of connective tissue increases small necroses appear and secondary calcification takes place The annulus fibrosus also is often affected The process starts at the base of the valves extends to the free edge and reaches the valvular surface Shrinkage of the connective tissue and calcification disturb the function of the valve and may cause insufficiency

Relative Incompetence Another type known to Corrigan is relative aortic insufficiency It is rare for the valvular ring itself to dilate and to cause incompetency in the presence of a normal valve even with the highest blood pressure values Relative aortic insufficiency is usually the result of marked damage to the myocardium or the aorta (Laubry and Doumer) It has been described in connection with myomalacia consequent to coronary sclerosis in fatty degenerative infiltration from anemia in aortitis without involvement of the valves (Maresch) and in hypertension Although some authors consider it a frequent event (Garrin) in our experience it is rare

Trauma Traumatic aortic insufficiency is also rare It occurs after direct or indirect trauma regardless of whether the valves are normal or abnormal Sudden physical strain in a patient with aortitis and syphilitic valvular changes may rupture a leaflet and lead to the sudden appearance of an aortic insufficiency These patients often present a musical diastolic murmur (sea gull murmur) which may be heard at some distance from the chest wall with the unaided ear The murmur is usually accompanied by a thrill Immediately after the provocative exertion severe pain is felt over the heart and the midsternal region the result of acute cardiac dilatation causing stretching of the pericardium This form of aortic regurgitation like the other types is more common in males It developed in one of our patients during a brawl and in another while he was playing soccer Both had syphilitic aortitis

Marfan s Syndrome In this congenital abnormality of the connective tissue which will be discussed more in detail in the chapter on congenital heart diseases insufficiency of the aortic valves occurs caused by changes in the aortic wall and valvular ring Dissecting aneurysms or rupture of the aorta are common

Symptoms

Paucity of Symptoms Most patients with aortic insufficiency have few symptoms In other valvular lesions especially those of the mitral valves dyspnea and palpitation appear quite early and many times the patient is aware of his cardiac disease long before decompensation occurs Patients with aortic insufficiency on the other hand remain asymptomatic for a long time For this reason the discovery of the lesion is often accidental — in the course of a periodic health examination after application for life insurance or upon examination by Army draft boards Such patients are often fully active they pursue ordinary sports and may even indulge in strenuous exertion without symptoms The diagnosis of an organic disease is consequently received with surprise

Freedom from complaints occurs even in patients who exhibit all the peripheral and auscultatory signs of the lesion that is marked backflow through the valve This situation is explained by the fact that the left ventricle is capable of full performance for many years even when increased demands are placed upon it The chief complaint of most cardiac patients is dyspnea Paroxysmal nocturnal as well as exertional dyspnea are absent in aortic insufficiency so long as there is complete compensation by the left ventricle accordingly the lesion is often entirely asymptomatic

Complaints may be absent for decades an aortic insufficiency which appeared after rheumatic fever in childhood may never produce symptoms or may cause them only at an advanced age This good prognosis and long duration of full compensation however are more often seen in the rheumatic type In syphilitic aortic insufficiency the prognosis is much poorer Naturally exceptions do occur we have seen patients with a syphilitic aortic insufficiency whose hearts did not change in size or shape and in whom no symptoms of decompensation appeared for more than a decade

The duration of compensation in any valvular lesion depends to a great extent on the condition of the myocardium and only to a slight degree upon the extent of the valvular lesion Patients with an extreme aortic stenosis or regurgitation may remain well provided the myocardium is normal On the other hand rapid and progressive decompensation takes place despite a minor valvular alteration when the heart muscle is damaged

Although the heart muscle is affected quite regularly in rheumatic fever usually the process is focal and heals completely without causing significant or permanent damage Only in occasional cases does failure set in early In syphilitic aortic insufficiency early myocardial damage is common largely because the orifices of the coronary arteries are narrowed heart failure thus appears usually at an early stage and often before the affected valves become markedly insufficient

Dyspnea The first complaint of patients with aortic regurgitation is as a rule paroxysmal nocturnal dyspnea which is typical for left ventricular failure Exertional dyspnea follows in accordance with the speed with which the left ventricle progressively fails and pulmonary stasis develops

Angina Pectoris A small percentage of cases with aortic insufficiency have real anginal pain It may occur even in children Often the distress develops while the patient is at rest or sleeping at night The pain may be tormenting While it responds readily to nitroglycerin frequently the relief is only temporary In this type of pain a paroxysmal rise of blood pressure has decisive importance The phenomenon will be discussed in the chapter on angina pectoris

Signs

Skin According to some clinicians patients with aortic insufficiency are so pale that the disease can be differentiated at first glance from mitral lesions Such a statement however is not in accord with the facts Patients with beginning

or advanced aortic insufficiency usually look perfectly normal and pallor certainly is not typical for this lesion If the patients are pale the chances are this can be traced to definite causes When the lesion is caused by syphilis a secondary anemia was seen following therapy with mercury or the arsenicals In rheumatic aortic insufficiency pallor may suggest continued activity of the rheumatic fever and therefore the temperature leukocyte count and the sedimentation rate should be checked The possibility of subacute bacterial endocarditis should be borne in mind

Pulse The examination of the patient should begin — as should the examination of all cardiac patients — with palpation of the pulse In a fully developed insufficiency of the aortic valve a pulsus celer et altus is found the pulse climbs and falls quickly and has a large amplitude The terms water hammer (a toy) pulse (quick ascent) Corrigan pulse and collapsible pulse (quick descent) are often employed The pulse seems abrupt and jerky

These changes of the pulse stem from many factors At the time the ventricle ejects its contents the arteries are emptier than normal due to the regurgitation of blood in diastole and peripheral vasodilatation The velocity of arterial blood flow is increased and the pulse wave climbs steeply The period of isometric contraction is distinctly shortened as is the ejection time a large volume of blood is therefore discharged within a short time The peripheral arteries are widened The diastolic backflow of blood causes a steeper descent of the pulse wave while the large stroke volume makes the pulse wave higher

This pulse however is not pathognomonic since it may be present without insufficiency of the aortic valve and it may be absent despite a regurgitation Other conditions with a similar abnormal mechanism present a Corrigan pulse It may be pronounced in persistent patent ductus arteriosus and in arteriovenous fistulas In the latter instance such a pulse may appear even when a small peripheral artery e g the temporal artery communicates with the accompanying vein

Furthermore this pulse is rather common in hyperthyroidism and in mild as well as in the fully developed Graves disease but the mechanism is somewhat different Hypermotility of the heart and arteriolar dilatation are the contributing factors The water hammer pulse is also encountered in many infectious diseases with high fever of varying origin such as pneumonia with vasomotor paralysis Patients with atheromatosis and aortitis may present this pulse even when the aortic valve is normal in these cases the elasticity of the ascending aorta is diminished and the contents of the left ventricle are expelled immediately into the peripheral vessels This pulse is often pronounced in beriberi even in the mild occidental form since thiamine deficiency disturbs muscular metabolism and changes the tonus of the vascular tree The ventricles are hyperactive A collapsible pulse may also be seen in severe anemias

If these disturbances can be ruled out (and usually this is a fairly simple matter) one may infer the diagnosis and — with the exercise of due care — even the degree of the lesion from the celerity of the pulse In uncomplicated cases the celerity of the pulse is proportional of the degree of regurgitation

Pulsus celer may be absent despite marked valvular insufficiency when an advanced mitral stenosis coexists In this case the stroke volume is small since the left ventricle is not well filled Under these circumstances none of the peripheral signs of an aortic insufficiency need appear The auscultatory signs may also vanish if there is a marked mitral stenosis It is obvious that an accompanying aortic stenosis will also abolish the peripheral signs of an aortic insufficiency The character of the pulse in this combined lesion depends upon the predominance of one lesion or the other It is not rare for the peripheral vasoconstriction in hypertension and nephrosclerosis to abolish the Corrigan pulse of an aortic insufficiency Finally in a terminal stage myocardial weakness may abolish the pulse changes

Whenever the examiner suspects the presence of a Corrigan pulse the radial artery should be palpated with the patient s arm raised perpendicularly In this position the characteristics of a water hammer pulse are more pronounced than *when the arm is horizontal not rarely the pulse seems normal unless the* arm is elevated Hydrodynamic factors (the summation of the pulse wave with reflected waves) seem responsible for this difference (Wiggers) It is also advisable to palpate the carotid artery which may show alterations of the pulse at an earlier stage than the radial artery this is explained by the size of the carotid artery and its proximity to the heart

The radial as well as the carotid pulse should be palpated on both sides to determine whether or not differences exist Not uncommonly there is some discrepancy in the size of the radial pulse in normal subjects This discrepancy *might be anticipated since the course of the radial artery is subject to anatomic* variations On the other hand the existence of distinct changes when both brachial or carotid arteries are compared is an important sign of the syphilitic form of aortic insufficiency In vascular syphilis the ostia of the innominate subclavian or left carotid arteries are often narrowed or even completely occluded In such a case one brachial or carotid artery may show little or no pulsation These pulse differences although often attributed to an aneurysm are simply the consequences of the syphilitic process in the aorta and in many cases permit the differentiation of the two major forms of aortic insufficiency

CAPILLARY PULSE Some observers assign far too much importance to the so called capillary pulse in the diagnosis of aortic insufficiency Our feeling is that this sign has no value It may be encountered in normal individuals a fact known to Quincke many healthy people show it on hot days or when a hand is placed in hot water in order to dilate the peripheral arteries (Lewis) It is also found in other disorders e g mitral lesions arteriosclerosis and hyperthyroidism and is therefore not characteristic Even the term capillary pulse is improper in view of the fact that the phenomenon may be noted without pulsation of the capillaries themselves That the phenomenon of capillary *pulsation* seen with the unaided eye derives from a different mechanism than the type observed with the capillary microscope is a source of much confusion

Other Peripheral Signs The other oft mentioned peripheral signs of aortic insufficiency have just as little practical importance as the capillary pulse Traube s sound Duroziez s double murmur Musset s sign and other phenomena are found when the water hammer pulse is present Most of these signs may be elicited whenever there is a marked peripheral vasodilatation and they are found in the absence of aortic insufficiency as in beriberi and hyperthyroidism

Blood Pressure The blood pressure shows characteristic alterations The diastolic regurgitation of blood into the left ventricle diminishes the diastolic pressure which usually reaches a level below 50 mm Hg Sometimes the diastolic pressure cannot be measured at all since the sound over the vessel remains loud down to zero The pulse pressure or amplitude the difference between systolic and diastolic pressure is increased but it should be stressed that the diastolic blood pressure is often equally low in other conditions such as hyperthyroidism beriberi arteriovenous fistulas and persistent patency of the ductus arteriosus On the other hand the diastolic blood pressure may remain high if the regurgitation is accompanied by a marked stenosis of the aortic valve or hypertension with nephrosclerosis In the condition last named a diastolic blood pressure of over 100 mm Hg is not rare despite a pronounced aortic insufficiency

There is no characteristic change of the systolic blood pressure in this lesion It may be normal despite an advanced aortic insufficiency Occasionally however it may attain a remarkably high level in both the rheumatic as well as the syphilitic form In one case of rheumatic aortic insufficiency we observed a systolic blood pressure of 320 mm Hg The hypertension is attributed to rapid arterial filling under increased force during the short ventricular systole which ejects a larger stroke volume Owing to the increased diastolic filling systole is more forceful in accordance with Starling s law The loss of elasticity of the ascending aorta particularly in the syphilitic type of aortic insufficiency also contributes to the systolic hypertension

In aortic insufficiency as well as in other cardiac lesions the blood pressure may rise in the course of cardiac failure (stasis hypertension)

HILL S PHENOMENON In aortic incompetency the blood pressure in the lower extremities is markedly higher than in the brachial arteries sometimes by as much as 80 to 100 mm Hg This is called Hill s phenomenon The same situation is encountered although less frequently in such other conditions as hyperthyroidism and arteriosclerosis The difference in systolic pressure between the arms and legs in normal individuals usually does not surpass 40 mm Hg This sign has always been somewhat puzzling because such differences in pressure would not be anticipated in a system of communicating tubes Actually with the use of a direct method for the registration of blood pressure in the lower extremities in cases of aortic insufficiency much smaller differences between the arm and leg readings are found than indicated above The Hill phenomenon is probably due partly to the fact that a larger mass of tissues surrounding the arteries of the lower extremities must be compressed when the blood pressure is measured partly to the higher kinetic energy of the blood in the large vessels of

the legs (Bazett Gladstone) The arteries for the arms and head depart at a right angle from the aorta whereas the femoral artery is a direct continuation of the abdominal aorta Therefore the velocity head due to systole is much higher in the arteries of the legs The Hill phenomenon does not seem to have any practical significance It is also found in arteriovenous fistulas (Lewis and Drury)

Apical Impulse The apical impulse is often heaving owing to hypertrophy of the left ventricle Due to left ventricular dilatation the apex beat may be displaced downward The fact that a large stroke volume leaves the thoracic cage within a short time leads to increased negativity of intrathoracic pressure and causes retraction of the interspaces over the precordial area (Lang)

Percussion and Roentgen Examination

Corresponding with the various stages of decompensation cardiac shape may assume one of three patterns (1) the heart may be normal in size and shape (figure 23 a) (2) it may show an aortic configuration with varying degrees of left ventricular dilatation (figure 23 b) (3) it may assume the shape of a mitralized aortic heart (figure 23 c) Establishing the size and shape of the heart by means of percussion or x ray has great value because this permits an evaluation of the various compensatory mechanisms in operation and also yields important prognostic information

(1) As just stated the heart may be normal in size and shape Naturally such patients are rarely encountered in hospital wards but they are often seen in private practice especially when presumably healthy individuals are examined (life insurance athletes military service) A heart of normal size can be found not only at the beginning or with a slight insufficiency but also in fully developed lesions of long duration and associated with all typical palpatory and auscultatory signs

The abnormal dynamic mechanism in an aortic insufficiency consists of blood returning from the aorta into the left ventricle during diastole The left ventricular content increases to the extent of the volume of regurgitated blood Different opinions prevail concerning the volume In the highest estimates about 50 per cent of the stroke volume (30 ml) flows back into the left ventricle when the valves are completely incompetent The increase of the diastolic ventricular content by 30 ml alone is inadequate to produce a cardiac enlargement distinctly perceptible and recognizable as pathologic Considerably larger amounts of fluid must accumulate for a pericardial effusion to be demonstrated clinically A moderate slowing of the heart rate within normal limits prolongs diastole The increment thus added to the usual ventricular contents far surpasses that of aortic insufficiency Furthermore the left ventricle in these cases empties normally in systole and there is no increase of residual blood Therefore it is reasonable to conclude that no clinically demonstrable enlargement of the left ventricle need occur solely from the abnormal valvular mechanism in aortic insufficiency

A 72 year old physician was observed who had developed an insufficiency of the aortic valve following rheumatic fever at the age of six. The diagnosis was made by a competent internist and was frequently confirmed in the course of sixty six years. Nevertheless the heart was normal in size and shape when the patient was last seen.

(2) A healthy myocardium can perform the increased work demanded of it by aortic insufficiency without unduly disturbing the circulation. However with incomplete emptying of the ventricle greater amounts of residual blood and dilatation appear early if the myocardium is damaged. Dilatation of the left ventricle appears with a rapidity proportionate to the state of this structure. If the myocardium in general is healthy no visible enlargement of the heart need



Fig 23 Three orthodiagrams obtained from patients with aortic regurgitation (a) Heart of normal size and shape (b) the heart shows an aortic configuration with a widened aorta (c) the heart is mitralized

appear for years. Early enlargement takes place when the heart muscle is damaged by either the rheumatic or the syphilitic process (coronary stenosis). One may conclude therefore with justification that if marked dilatation occurs with considerable speed the myocardium is injured even in the absence of other signs. The state of the myocardium and not the extent of the valvular lesion determines the size of the heart. As a matter of fact enormous cardiac enlargement (cor bovinum) otherwise observed only in hypertension may be encountered in the late stages of aortic insufficiency. It is clear from this discussion that the rapidity with which the left ventricle enlarges in aortic insufficiency has definite prognostic significance.

Since the strain is on the outflow tract of the left ventricle in accordance with the rules discussed before the heart first becomes elongated and the apex beat is displaced downward. There is no widening of the heart. Later the apex becomes rounded the heart is somewhat more plump and with increasing dilatation of the left ventricle the waist of the heart becomes more pronounced leading to the typical aortic configuration (figure 23 b). The patient may be asymptomatic and normally active even when the enlargement of the left ventricle has reached a remarkable degree.

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Corresponding with the various stages of decompensation cardiac shape may assume one of three patterns (1) the heart may be normal in size *and shape* (figure 23 a) (2) it may show an aortic configuration with varying degrees of left ventricular dilatation (figure 23 b) (3) it may assume the shape of a mitralized aortic heart (figure 23 c) Establishing the size and shape of the heart by means of percussion or x ray has great value because this permits an evaluation of the various compensatory mechanisms in operation and also yields important prognostic information

(1) As just stated the heart may be normal in size and shape Naturally such patients are rarely encountered in hospital wards but they are often seen in private practice especially when presumably healthy individuals are examined *(life insurance athletes military service) A heart of normal size can* be found not only at the beginning or with a slight insufficiency but also in fully developed lesions of long duration and associated with all typical palpatory and auscultatory signs

The abnormal dynamic mechanism in an aortic insufficiency consists of blood returning from the aorta into the left ventricle during diastole The left ventricular content increases to the extent of the volume of regurgitated blood Different opinions prevail concerning the volume In the highest estimates about 50 per cent of the stroke volume (30 ml) flows back into the left ventricle when the valves are completely incompetent The increase of the diastolic ventricular content by 30 ml alone is inadequate to produce a cardiac enlargement distinctly perceptible and recognizable as pathologic Considerably larger amounts of fluid must accumulate for a pericardial effusion to be demonstrated clinically A moderate slowing of the heart rate within normal limits prolongs diastole The increment thus added to the usual ventricular contents far surpasses that of aortic insufficiency Furthermore the left ventricle in these cases empties normally in systole and there is no increase of residual blood Therefore it is reasonable to conclude that no clinically demonstrable enlargement of the left ventricle need occur solely from the abnormal valvular mechanism in aortic insufficiency

tion of the aortic valve Whenever the diastolic murmur is heard best in this area the ascending aorta is markedly dilated and therefore moves near the chest wall The murmur is thus transmitted from the aortic valve to the second right intercostal space by the dilated aorta Conversely the more the murmur is transmitted toward the right shoulder the greater the aortic dilatation Since marked dilatation of the ascending aorta usually occurs in the syphilitic type the diastolic murmur of syphilitic aortic insufficiency is in most cases heard best over the second right intercostal space In the rheumatic form and especially when the aortic insufficiency is accompanied by a mitral lesion the murmur is heard best along the left lower sternal border as mentioned before Naturally there are exceptions to all rules no one should attempt to establish the etiology

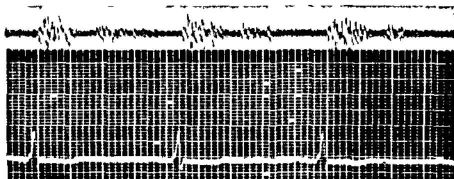


Fig 24 Rough systolic and high pitched diastolic murmur registered over the second right intercostal space near the sternum in a 54 year old man with syphilitic aortic regurgitation

of the lesion solely on the point of maximum intensity of the diastolic murmur In some cases of syphilitic aortic insufficiency the aorta does not dilate abnormally and the murmur is audible only at the lower sternal border Sometimes in rheumatic aortic lesions a combined insufficiency and stenosis of the valves causes the ascending aorta to enlarge markedly and the diastolic murmur to be heard best in the second right intercostal space Nevertheless in most cases the location of the diastolic murmur is a valuable aid in differentiating the two main types of aortic insufficiency

As previously mentioned the diastolic murmur may disappear in aortic insufficiency if accompanied by an advanced mitral stenosis or a tricuspid regurgitation

In rare cases (usually but not invariably in syphilitic aortic insufficiency) the diastolic murmur may be chirping mewing or cooing (sea gull murmur) This cooing like the sound of a cuckoo clock may be due to a tearing of the valve and actually appears not rarely in traumatic aortic insufficiency An explanation of this phenomenon may be retroversion of the right aortic valve toward the chamber (Bellet et al)

The systolic murmur which develops early in the syphilitic type of aortic regurgitation and which sometimes appears later in the rheumatic form may be very rough and harsh and may last throughout systole In other cases it is soft and distant When accompanied by a thrill it may be confused with the *murmur of aortic stenosis While aortic stenosis never occurs in the pure syphilitic* lesion it may be present when rheumatic and syphilitic changes in the valve are simultaneously present

The old conception that roughness of the aortic wall or valves is responsible *for the murmur has been rightly relinquished Since the blood flows mainly in* the center of the vessel mural friction scarcely comes into consideration as the cause of the systolic murmur The following explanation is probably more accurate Blood is forced from a dilated left ventricle into a dilated aorta through a ring of normal diameter This acts as a relative stenosis and the abnormal *turbulences and eddies create a murmur Actually* a similar murmur always develops over the aorta when the left ventricle and aorta are dilated (hyper tension myocardial lesion heart block with brady cardia and an increased stroke volume) In aortic insufficiency the acceleration of the systolic blood flow due to greater filling of the left ventricle may participate in the development of the systolic murmur



Fig 25 Sketch to demonstrate the transmis sion of a systolic aortic mur mur to the apex (hourglass murmur)

The point of maximum intensity of this sys tolic murmur is located at the classical site for *auscultation of the aortic valve that is paraster* nally in the second right intercostal space If the murmur is sufficiently loud it is transmitted to the neck vessels All systolic aortic murmurs however have a second point of maximum intensity which is situated at the cardiac apex If the stethoscope is moved slowly from the second right intercostal space toward the cardiac apex the murmur becomes progressively softer over the right ventricle and then gradually grows louder as the apex is approached Apparently the murmur is transmitted to the apical area along the interventricular septum Systolic aortic murmurs are called hourglass murmurs since graphic representation of the two points of maximum intensity portrays the form of an hourglass (figure 25)

The presence of a loud systolic murmur over the apical area occasionally leads to the mistaken diagnosis of mitral insufficiency This diagnosis seems supported by the fact that the systolic murmur over the apex may sound entirely different from that over the aorta Nevertheless an alteration of the acoustic properties does not mean a different origin or mechanism of the murmur Murmurs may be filtered and modified by the transmitting tissues some vibrations are transmitted well some poorly while others are lost completely

Not rarely the upper point of maximum intensity disappears and no murmur is heard at the base while the loud systolic murmur persists over the apex This

is also wrongly interpreted as a mitral murmur The possibility of its transmission from the aorta is often forgotten This situation usually arises in patients with emphysema in whom the heart and ascending aorta are covered by lung At the apex where the left ventricle approaches the chest wall the murmur is audible Naturally in these cases the heart sounds disappear parasternally at the second right interspace

If the emphysema is more pronounced and the heart more thoroughly covered by lung cardiac auscultatory phenomena disappear even at the apical area in this instance heart sounds and murmurs are audible only over the lower end of the sternum near the xiphoid and often even more caudad

In an aortic insufficiency with marked dilatation of the left ventricle a relative mitral regurgitation often develops as described above The mitralization of the heart then progresses more rapidly a new systolic murmur appears over the apex and the second pulmonic sound becomes more accentuated

In some instances of rheumatic or syphilitic aortic insufficiency a tripartite murmur is heard between the apex and the lower end of the sternum It is composed of one systolic and two diastolic murmurs The reason for duplication of the diastolic murmur is unknown to us Both parts have the same intensity and seem practically identical The rhythm is like that found in gallop rhythm except that the sounds are replaced by murmurs

Austin Flint Murmur Occasionally in aortic insufficiency a presystolic or rumbling diastolic murmur is heard over the apex causing confusion with mitral stenosis This murmur the Austin Flint murmur is regarded by some as very common and is said to occur in 50 per cent of the cases We have found it to be uncommon Inexperienced physicians often confuse an impurity of the first or second heart sound with a murmur and make the diagnosis of mitral stenosis or Austin Flint murmur As a matter of fact it has been shown recently that a variety of acoustic phenomena may simulate the murmur of mitral stenosis in cases of aortic regurgitation (Luisada) With experience graphic registration is not necessary for differentiation

Many explanations have been advanced for the Austin Flint murmur Some believe that the diastolic influx of blood from the aorta causes the mitral valves to float if the floating leaflets are pushed close to the mitral orifice they may impede the atrial blood entering the ventricle Others think that the murmur is especially apt to occur in those cases of aortic insufficiency in which the aortic cusp of the mitral valve is forced back by blood regurgitating from the aorta this is said to hamper the inflow of blood from the atrium Another group believes that the murmur is created by the meeting of the two blood streams one from the left atrium and the other from the aorta

An unequivocal differentiation between this functional mitral stenosis the presumptive cause of the Austin Flint murmur and true mitral stenosis is possible only at necropsy

The character of the heart sounds lacks significance in the appraisal of the degree of aortic insufficiency Owing to left ventricular hypertrophy the first

heart sound at the apex may be very loud but it may also be submerged in or indistinguishable from the systolic murmur Likewise the second heart sound may be absent or faint in advanced cases as well as in early cases when the to and fro murmur is heard instead of the heart sounds Even with a well advanced aortic insufficiency the second sound may have a ringing tone We have seen one case in which two of the aortic leaflets were completely destroyed by bacterial endocarditis and only one half of the third leaflet functioned A very loud second aortic sound was heard until the end

The intensity of the second sound offers no assistance in the differential diagnosis between rheumatic fever and syphilitic aortic insufficiency

Occasionally when aortic insufficiency is severe and the water hammer pulse is pronounced a very loud sound is noted at the base of the heart with its greatest intensity in the supra and infraclavicular region It is usually confused with the first heart sound actually however it is not of cardiac origin Rather it is produced by systolic distention of the large arteries near the base of the heart and corresponds to the vascular sounds audible over the peripheral arteries in such cases

Rhythm The rhythm is usually regular atrial fibrillation is rather the exception

Rate The rate is often rapid This sinus tachycardia is prone to occur in young individuals rates of 120 per minute being not uncommon The tachycardia sometimes occasions the use of digitalis which is not indicated in a sinus tachycardia of this type The low mean arterial pressure in aortic insufficiency causes the tachycardia with the aid of a carotid sinus reflex The significance of this acceleration was recognized by Corrigan more than a century ago but thinking somewhat teleologically he regarded it a compensatory measure the tachycardia by shortening the duration of diastole reduces the amount of regurgitating blood

Electrocardiogram

In early uncomplicated cases the electrocardiogram shows only a left axis deviation more advanced cases present the pattern of left ventricular hypertrophy as in hypertension

Complications

With the exception of angina pectoris the most serious complication is subacute bacterial endocarditis If the patient with aortic regurgitation develops fever weakness loss of appetite and anemia this ominous complication should be suspected

Differential Diagnosis

While the diagnosis is easy in a fully developed pure aortic insufficiency it may be difficult when mitral or aortic stenosis coexists Earlier it was pointed out that all peripheral and auscultatory signs of an aortic insufficiency may disappear in such cases sometimes the correct diagnosis is possible only when

the results of the roentgen examination are correctly evaluated Thus a wide aortic knob showing strong pulsations may lead to the correct diagnosis of an unrecognized aortic insufficiency in the presence of a mitral lesion

A diastolic murmur at the same place and with the same characteristics is sometimes heard in mitral stenosis when a relative insufficiency of the pulmonary valve appears (Graham Steell murmur) The differentiation will be discussed later

Difficult occasionally is the differentiation from a patent ductus arteriosus or aneurysm of the sinus of Valsalva which has ruptured into a ventricular cavity The condition of patients with the latter condition rapidly deteriorates and death soon follows Usually in both of the above mentioned conditions there is a continuous murmur with systolic accentuation A systolic murmur followed by a diastolic one over the pulmonary artery appears in patients with atrial septal defects

Diastolic murmurs in the same area as those of aortic insufficiency are sometimes heard in hyperthyroidism In such patients the differentiation may be difficult since both conditions produce the same peripheral signs

In a cardiac aneurysm a soft high pitched diastolic murmur is sometimes audible to the left of the sternum, this murmur may be confused with the murmur of aortic insufficiency until necropsy reveals the correct diagnosis (Scherf and Brooks) Peripheral signs of aortic regurgitation are absent

The most important problem in the differential diagnosis is the distinction between the rheumatic and syphilitic type of aortic insufficiency Very often the history throws no light on the situation In many cases a history of syphilis cannot be obtained for a variety of reasons The serologic tests are not decisive for up to 15 per cent of patients with luetic aortic insufficiency have an entirely negative serology About 40 per cent of the rheumatic cases are unaware of a previous attack of rheumatic fever

Two points mentioned during the discussion of symptoms and signs may be of value

(1) The presence of a marked difference in the strength of the brachial or carotid pulse between the two sides is a strong argument in favor of a syphilitic aortic insufficiency

(2) If the murmur is heard best over the second right intercostal space and particularly toward the right shoulder pronounced dilatation of the ascending aorta and therefore syphilitic aortic insufficiency should be suspected

Undoubtedly in a certain number of patients the differential diagnosis is impossible

Prognosis

As pointed out earlier the prognosis depends mainly on the status of the heart muscle Since myocardial damage during rheumatic fever is rarely very pronounced the outlook for patients with a rheumatic aortic insufficiency usually is rather good The frequent concurrence of coronary orifice stenosis in the syphilitic form necessitates a more guarded prognosis While some statistics suggest

that the average duration of life from the beginning of symptoms may approximate two years in syphilitic aortic insufficiency the process may come to a standstill at any time and complete compensation for 15 or more years occurs Nevertheless the prognosis is certainly more serious than in the rheumatic type

Surgery

Surgical therapy of aortic regurgitation is only in its infancy and further developments may be expected (Hufnagel)

The Hufnagel plastic (lucite) valve leads to hemolytic anemia because of the mechanical destruction of red cells

A traumatic aortic insufficiency was found in a 17 year old man who had been kicked in the chest by a horse and became unconscious A plastic aortic valve was inserted and the patient was symptom free and working 14 months after the operation (Leonard et al)

STENOSIS OF THE AORTIC VALVE

Incidence

Stenosis of the aortic valve (aortic stenosis) is a common valvular lesion This fact must be stressed because it contradicts the opinion which prevailed widely until a few years ago To be sure the diagnosis often is made only when the lesion is rather advanced the diagnosis of a moderate stenosis may be difficult The lesion is more common in men than in women the ratio being 3 to 1 (Kumpe and Bean)

Etiology

Rheumatic Fever In a majority of cases aortic stenosis results from rheumatic fever causing endocarditis in which the aortic valves fuse usually an insufficiency accompanies a stenosis Rheumatic aortic stenosis without insufficiency is very rare but the latter is often not diagnosed because of the absence of peripheral signs and murmurs

Atherosclerosis The occurence of another form of aortic stenosis the atherosclerotic type is established but its frequency is at present not fully determined Karsner thinks that rheumatic fever is responsible for the majority of advanced aortic stenoses while others maintain that atherosclerosis is responsible in most instances The atherosclerotic process begins at the base of the valve in the sinus pocket and slowly advances to the free edge that is in a direction opposite to that occurring in rheumatic fever Since many patients with rheumatic aortic stenosis live to an old age since lime salts are commonly deposited in the valves following rheumatic verrucous endocarditis and since a positive history of rheumatic fever may be absent in rheumatic aortic stenosis an atherosclerotic aortic stenosis is frequently diagnosed in patients with rheumatic valvular disease This mistake is understandable in view of the fact that as emphasized in the original description of atherosclerotic aortic stenosis the ascending aorta in these cases need not show evidence of atherosclerosis

Congenital Congenital stenosis of the aortic orifice due to a malformation is not rare It may involve the conus of the left ventricle the aortic orifice itself or the supravalvular aorta

As mentioned above syphilis never causes aortic stenosis The presence of syphilitic aortitis or regurgitation therefore precludes the existence of an aortic stenosis unless an additional rheumatic valvulitis exists

Mechanism

Stenosis of the aortic valve is easily compensated As in hypertension the augmented resistance increases the residual blood the diastolic filling and thus the initial stretch of the fibers of the left ventricle This causes increased energy of contraction and hypertrophy Since the stenosis progresses gradually there is ample time for these changes to develop The hypertrophy may assume great dimensions in aortic stenosis Animal experiments have shown that the aortic orifice must be reduced to less than one quarter its normal size before the output diminishes and changes of blood pressure and pulse appear (de Heer) Even under physiologic conditions the valves approximate rather closely during a great part of systole and permit only a small opening The normal aortic orifice is about 2 0 square centimeters in area In confirmation of the experimental findings Gorlin et al found that an aortic orifice of 0 5 cm is critical since it makes necessary a high intraventricular pressure (up to 200 mm Hg) The isometric contraction period like the ejection period is slightly prolonged

Symptoms

The adjustment of the circulation to the lesion is usually so complete that patients with extreme aortic stenosis may pursue athletic activities and may undertake arduous physical strain without symptoms Naturally here as in other valvular lesions a healthy myocardium is the necessary prerequisite

The excellent compensation of aortic stenosis makes it understandable why patients are sometimes encountered who had an aortic stenosis since early childhood the first symptoms of which appeared only when they were 60 years old or later Patients may even be over 70 when the first evidence of left ventricular failure due to aortic stenosis appears Cheyne Stokes respiration and paroxysmal nocturnal dyspnea are the first signs of decompensation

Some patients however develop symptoms very early in the disease at a time when full compensation prevails They complain of fainting and anginal pain

Syncope Attacks of syncope and loss of consciousness may follow brisk movements and sudden change of posture or overexertion (Gravier Callavardin) Often they appear without any visible reason Even epileptiform convulsions occur causing these patients to be treated for epilepsy until the real reason for the attacks is discovered Contrary to frequent statements such attacks also occur at rest and even during sleep

The attacks are not rare for syncope was noted in 31 of 235 cases of aortic stenosis (McGinn and White) Hammarsten found syncope in 16 of 63 subjects

with aortic stenosis Unconsciousness may last from a few minutes to a half hour The convulsions are not as a rule generalized Few studies of the pulse rate facial color or blood pressure during the attacks are available since the episodes recur too infrequently to permit observations and records Marked arrhythmias were found in electrocardiograms taken during an attack of syncope it seems however that the syncope appears before the arrhythmia The latter is not marked enough to cause unconsciousness

The mechanism of these attacks is not satisfactorily explained A cerebral ischemia is probable but unproven the long duration of some episodes however makes a profound cerebral ischemia dubious There are no sequelae recovery is prompt and complete This and the absence of aura help in the differentiation from epilepsy It has been suggested that the syncope of aortic stenosis might be due to some disturbed carotid sinus reflex mechanism Pressure on the carotid sinus of such patients however does not initiate an attack and the responses are not abnormal Nevertheless it is conceivable that the carotid sinus in these patients responds abnormally to physiologic stimuli such as a sudden fall of blood pressure consequent to dilatation of the splanchnic vessels Thus regulation of the blood pressure level is disturbed

Anginal Pain This is another typical complaint Kumpe and Bean noted cardiac pain in 37 per cent of their cases The pain often radiates in the usual manner to the left arm and appears on exertion or excitement like the classic angina on effort In addition it often awakens the patient from deep sleep Its mechanism will be discussed later in the chapter on angina pectoris

Signs

Pulse In advanced cases the pulse shows definite changes the exact opposite to the pulsus celer et altus of aortic regurgitation It is called pulsus parvus be cause of its small size in button hole aortic stenosis even the carotid pulse is scarcely palpable It is also called pulsus tardus because of its slow rise The pulse is often anacrotic While the blood pressure is often low we have frequently found normal values and hypertension is not less common than in the average population The auscultatory gap (see chapter on hypertension) is usually found during the auscultatory measurement of the blood pressure

Palpation A heaving apex beat may be felt since the left ventricle is hypertro phic This sign however is often missed In most cases a systolic thrill is palpable over the aortic area in the second right interspace and also over the carotid vessels partic ularly on the right side It is common because of the low pitch of the murmur in aortic stenosis Sometimes it can be palpated only in deep expiration and when the patient sitting or standing bends forward slightly It is absent with pulmonary emphysema A similar thrill however may be present whenever a rough systolic murmur arises at the same place therefore it may occasionally be noted in atheromatosis and syphilitic aortitis The systolic thrill is also found over the apex and may be located exclusively there when emphysema prevents its palpation over the aorta

Percussion and Roentgen Fxamination Both methods often fail to reveal any enlargement of the left ventricle for many years even when the lesion is advanced This is explained by the fact that the primary change is hypertrophy which starts at the outflow tract of the left ventricle Dilatation which may not appear until late proceeds along the axis of the left ventricle displacing the apex beat downward This displacement is often missed during the examination when the apex beat is not felt and the cardiac shadow merges with the abdominal shadow Enlargement of the heart along the transverse diameter causing the aortic configuration is a late event

On x ray examination but rarely on percussion an unusual widening of the aorta is found involving the initial portion of the ascending aorta This finding is surprising since the small pulse and slow ejection of blood might lead one to expect the aorta to be less dilated than it is for instance in aortic insufficiency If one has the opportunity to examine at necropsy a patient whose aorta seems to have been markedly dilated during life every sign of dilatation may be absent This suggests that the dilatation is dynamic Due to the great force with which the blood is ejected through the stenotic valve by the hypertrophied left ventricle a jet action is present and dilatation of the aortic wall is produced In two cases of aortic stenosis with superimposed subacute bacterial endocarditis we found an endarteritis at autopsy Vegetations were implanted in the aortic wall just where one would assume that the blood coming from the left ventricle struck the side of the vessel and caused a lesion of the endothelium Schnoor et al expressed the opinion that turbulences and repetitive pulsatile stresses cause a structural fatigue and dilatation

Careful fluoroscopy reveals calcification of the aortic valves in many cases This finding greatly supports the diagnosis Pyke and Symens who examined radiologically 400 males over 60 years of age found calcifications of the mitral valve in 2 75 per cent and of the aortic valves in 3 5 per cent It is necessary to differentiate valvular calcifications from those in the pericardium and myocardium (following necrosis in myocardial infarction) and calcium deposits in old mural thrombi Calcification occurs rather often in elderly subjects in the annulus fibrosus of the valve (the cardiac skeleton) (figure 26)

Sosman recommended certain rules that should enable one to distinguish between mitral and aortic valve calcifications The former are situated more toward the apex in the antero posterior picture in the left anterior oblique position when the heart just clears the spine the mitral valves are in the posterior third of the cardiac shadow while the aortic valves are in the middle third Valvular calcifications are C or J shaped and linear or diffuse

Auscultation A rough systolic murmur is usually found over the second right intercostal space This murmur radiates to the neck vessels and also to the apical area It sounds very close to the ear is prolonged and may fill all systole In some cases it is short and resembles the murmur heard in atheromatosis or aortitis Kumpe and Bean found it in only 83 per cent of proved cases In phono cardiograms one finds that the vibrations gradually increase in size and after

reaching a maximum height decrease (diamond shaped murmur) Figure 27 shows this murmur registered over the second right intercostal space in a 32 year old patient with aortic stenosis Similar murmurs are found in pulmonary stenosis and some congenital heart lesions



FIG 26 Atheroma of the aorta with calcium deposits in the arch and calcification of *the heart skeleton*

Quite characteristically either the systolic murmur of aortic stenosis is not followed by a second sound or else the second sound is distant This is understandable if one recalls how the valves are transformed into a firm calcified ring in which the individual cusps are no longer discernable closure of these valves at the end of systole therefore is impossible However the second pulmonic sound may be heard over the second right intercostal space A normal second aortic sound is heard in patients with an infravalvular congenital aortic stenosis In



Fig 27 Diamond shaped murmur obtained over the second right intercostal space parasternally in a patient with rheumatic aortic stenosis

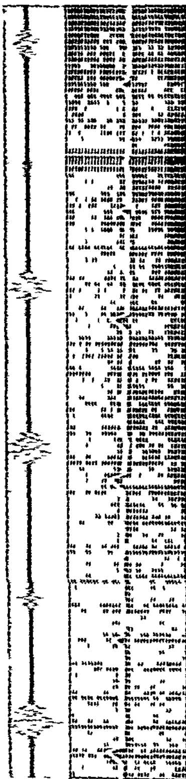


Fig 28 The systolic diamond shaped murmur in a patient with aortic stenosis is louder the longer the preceding diastole

such cases the systolic murmur may be heard only over the left second or third intercostal space to the left of the sternum The loud systolic aortic murmur becomes distinctly softer when the strength of the left ventricle diminishes and louder when the condition of such a heart is improved by digitalis We have seen button hole stenoses of the aortic valves become silent with heart failure In such cases no sounds or murmurs are audible over the aorta Its loudness depends on the diastolic filling of the left ventricle (figure 28) The peripheral arteries scarcely pulsate but the patient may be able to walk without dyspnea and he can lie flat *in bed without orthopnea*

A diastolic murmur of aortic regurgitation — if present — supports the diagnosis It is inaudible in about 50 per cent of the cases When present it is heard usually at the lower left sternal border Being often very faint it is easily missed

A systolic apical murmur is always present Usually it is a transmitted aortic murmur but in advanced stages of dilatation of the left ventricle it may be caused by a relative mitral insufficiency

Arrhythmias are rare An unexplained bradycardia is as common as the tachycardia of aortic regurgitation This is fortunate because the prolongation of diastole (and partly also of systole) is advantageous in the presence of an aortic stenosis This bradycardia however is often deceptive and may dissuade the *physician from giving digitalis if necessary*

A systolic click (claquement aortique protosystolique) appearing 0 06 to 0 08 second after the onset of the first heart sound has been described

Electrocardiogram In late stages the electrocardiogram shows evidence of left ventricular hypertrophy Because of the elongation of the heart (egg shaped) and due to the dilatation of the outflow tract only left axis deviation is often missing and only inverted T waves appear in the standard leads

Differential Diagnosis

If there is a characteristic pulsus tardus a systolic thrill and a loud prolonged systolic murmur over the aorta and the second aortic sound is absent the diagnosis of aortic stenosis is easy This is particularly true if the heart shows the anticipated configuration and the patient complains of fainting spells and anginal pain

The diagnosis and differentiation from other conditions will be difficult if the lesion is less advanced Sometimes it will be impossible to decide whether a rheumatic aortic insufficiency with a slight stenosis of the valves exists or whether we are dealing with a pure aortic insufficiency In syphilitic aortic insufficiency the systolic aortic murmur may be very loud and a thrill may even be palpable over the aorta In the average case of syphilitic aortitis however the second aortic sound is loud in elderly people with emphysema on the other hand the second aortic sound may become inaudible in a normal heart and this makes differentiation difficult

When there is no evidence of aortic regurgitation the differentiation between an aortic stenosis and atheromatosis or aortitis may be difficult It is not unusual to suspect atheromatosis in a patient of 70 years or more and to find an aortic stenosis of rheumatic origin at necropsy In this case as well the presence or absence of an accentuated second aortic sound within certain limits may help in the differentiation

An aortic stenosis may also be overlooked if it occurs in a patient with an advanced mitral stenosis for the mitral lesion may dominate the clinical picture

Catheterization Confirmation of the diagnosis by catheterization of the left ventricle although possible is not without risk and therefore is better omitted The catheter must be introduced via a peripheral artery Its introduction into the left ventricle may be difficult It may obstruct completely the very small lumen of the aortic orifice A very high systolic blood pressure in the left ventricle with a much lower one in the aorta is characteristic

Prognosis

The excellent prognosis of the lesion and the long duration of full compensation has often been stressed Many patients with aortic stenosis live active lives without ever knowing that they have any heart disease The average age reached by patients with pure aortic stenosis is 65 years (Mitchell et al) This includes of course patients who developed the lesion late in life because of atherosclerosis Grant alone comes to a different conclusion and calls the prognosis of aortic stenosis least favorable

Patients with aortic stenosis may die suddenly This event was noted in 6 of 28 observations (Cabot) and it occured in 9 of 11 cases in another group (Marvin and Sullivan) It seems probable that the sudden death is in some way associated with the attacks of loss of consciousness or the anginal pain due to myocardial ischemia The latter may induce ventricular fibrillation

Surgery

Surgical therapy of aortic stenosis with the finger fracture method was recommended as early as 1913 (Tuffier) The operation has been revived in recent years and with progress in surgical technic it may bring success Because of the frequency of calcification of the valves surgery cannot always yield a good result In view of the good prognosis of most cases the operation should be reserved for those patients with progressive stenosis of the aortic valves in which anginal pain syncope or failure of the left ventricle make the outlook without surgery rather dubious The approach from the ventricle is difficult as compared to pulmonary stenosis where it is employed with success This depends upon the great thickness of the left ventricle and the very high pressure within it According to one proposal a dilator should be introduced from the apical area of the left ventricle The mortality is still near 16 per cent but diminishes gradually as better technics are developed A transaortic approach at present seems to provide better

results and a lower mortality Baker and Campbell had 6 deaths in 16 operated patients good results were obtained only in five The greatest danger is creation of an aortic regurgitation Personal experience taught us that in dog experiments with the heart exposed in situ creation of such a lesion during an attempt at severing the left bundle branch leads to an immediate tremendous dilatation of the left ventricle and cardiac standstill

MITRAL STENOSIS

Mitral stenosis one of the most common valvular lesions is often combined with mitral insufficiency Observations during surgery reveal however that not rarely the stenosis is pure For didactic reasons only the latter type of mitral stenosis will be considered here

Etiology

Apart from very rare congenital malformations which cause atresia or narrowing of the mitral orifice traumatic mitral stenosis and rare instances of a healed bacterial endocarditis the etiology of the lesion is always rheumatic fever A previous history of rheumatic fever to be sure cannot be obtained in about 40 per cent of the cases These patients deny having had joint manifestations chorea or tonsillitis and even report that they have never suffered from a febrile disease

Two forms of congenital mitral stenosis exist A child may be born with a rheumatic mitral stenosis In such cases we may assume that the mother had rheumatic fever during pregnancy In the other type actual malformation of the mitral valves exists and defects of the atrial septum coarctation and aortic stenosis usually are also present (Ferencz et al)

Age Sex Owing to the relationship to rheumatic fever the maximum incidence of mitral valve disease is between the ages of 10 and 40 although many cases are observed in younger or older individuals Mitral stenosis was treated successfully by surgery in a child three years old Females seem more prone to develop rheumatic mitral disease this is especially true for mitral stenosis

Pathology

The rheumatic process discussed in a previous chapter leads to fusion of the mitral leaflets with thickening and secondary calcification in an appreciable number of cases This process usually accompanied by shortening and fusion of the chordae tendineae may be only just discernible or very severe In an advanced case of mitral stenosis the orifice is so narrowed and distorted that it is compared according to its shape with a button hole or fish mouth If the shortening of the chordae tendineae displaces the orifice toward the apex a funnel form of the mitral orifice is found at postmortem examination Sometimes an extensive calcification may involve the entire ring

Pathophysiology

Dynamic changes appear only in a rather advanced experimental stenosis since slight alterations are easily overcome by compensatory mechanisms In experimental mitral stenosis reduction of the mitral orifice to one quarter of its natural size is necessary before the resistance becomes so high that the rise of pressure in the left atrium is unable to compensate for it A valvular area of 1 square cm is critical since a pressure head to guarantee a normal cardiac output is necessary that is greater than the osmotic pressure of the plasma proteins Blood pressures of 160 mm Hg have been measured in the pulmonary artery with an intracardiac catheter That is 8 times the normal pressure A hydraulic formula has been given which permits one to calculate the area of the mitral valve orifice in diastole The rise of pressure within the left atrium leads to hypertrophy and later to dilatation of this chamber The pressure within the lesser circuit also rises early and increases the strain on the right heart Filling of the left ventricle decreases and leads to an atrophy which involves mainly its inflow tract

The volume of intrathoracic blood rises but slightly as opposed to left ventricular failure where it is markedly increased The progressive vascular changes in the lesser circuit in mitral stenosis are responsible for this There is at first a marked functional narrowing the cause of which is local anoxia (see Cor pulmonale) later organic changes of the vessels occur (see below) Pulmonary and bronchial arteries anastomose with each other and the pulmonary veins are overloaded The bronchial arteries show a marked hypertrophy of the media The pressure in the pulmonary capillaries and in the left atrium is estimated by pushing the tip of a catheter into a small pulmonary artery

The lesion develops slowly and its evolution requires at least six months and often longer before it can be recognized

Symptoms

The patient may have few complaints Not rarely mitral stenosis is found accidentally and the patient denies any symptoms relating to the lesion This situation occurs more frequently than in aortic insufficiency but such cases are known to every physician Careful interrogation may reveal that the capacity for exertion has always been somewhat reduced and rapid climbing of stairs or walking uphill has provoked dyspnea and palpitation Since however similar symptoms may appear in the absence of valvular lesions in healthy people especially in the obese and since the symptoms remained stationary the patient never consulted a physician nor complained of his condition Once in a while the physician sees such patients who have had mitral stenosis for at least 30 to 40 years come for a routine physical examination and assert they feel absolutely normal Occasionally a woman who has had a mitral stenosis since childhood seeks medical advice for the first time during or after the menopause when cardiac complaints typical for the climacteric develop At other times mitral stenosis is discovered during pregnancy or when a subacute bacterial endocarditis develops

Dyspnea In the majority of cases in contrast to the lesions of the aortic valve symptoms appear early While the left ventricle can maintain compensation for a long time in an aortic lesion in mitral stenosis the burden of compensation falls upon the left atrium The latter is equal to this task only in the presence of a very slight stenosis Even when the left atrium is able to force sufficient blood through the narrowed orifice at rest this becomes impossible when the demands are increased by physical exertion Stasis in the left atrium and engorgement in the lesser circuit appear with shortness of breath at first only upon severe exertion but later even on minimal activity In some cases the lungs become engorged so quickly on exertion excitement or the increase of rate that severe attacks of pulmonary edema appear Dyspnea may be so severe that any physical effort is difficult and the patient is forced to remain in a sitting position due to orthopnea

Patients with mitral stenosis do not have cardiac asthma or Cheyne Stokes respiration unless complications exist which lead to left ventricular failure Pulmonary edema is not too rare but it is a special type which has been discussed in the appropriate chapter

In recent literature the statement is often encountered that paroxysmal nocturnal dyspnea occurs in patients with pure mitral stenosis If one interprets this phrase to mean dyspnea appearing suddenly at night it is correct An exciting dream or sexual intercourse may cause dyspnea at night or the patient may slide down from his pillows and become dyspneic If by the term paroxysmal nocturnal dyspnea one understands the well defined forms of dyspnea discussed in the first chapter of the present volume then it must be said that patients with mitral stenosis are singularly free from this form of dyspnea It has never become clear to us why mitral stenosis with the marked reduction of cardiac output does not show the several forms of paroxysmal dyspnea such as cardiac asthma and Cheyne Stokes respiration

For obvious reasons digitalis is useless for the treatment of pulmonary edema in mitral stenosis The use of mercurial diuretics and morphine — given prophylactically — in minute amounts (15 to 20 drops of a 1 per cent solution of morphine hydrochloride in water or a 50 mg tablet of Demerol prior to sexual intercourse) may prevent the attack

Palpitation This symptom appears in the early stages It is noted more frequently at night and awakens the patient No satisfactory explanation for this phenomenon is known and the reason for its frequent occurrence in mitral stenosis are equally obscure The quick systole due to incomplete filling of the left ventricle may contribute to the sensation of palpitation

In hyperthyroidism and in cardiac neuroses palpitation may be due to increased rate and hypermotility of the heart The rate alone however does not seem to be a decisive factor in evoking this symptom for palpitation may be absent in a paroxysmal tachycardia when the rate is over 250 and it may also be absent despite marked pounding of the chest wall by cardiac pulsations

It is not rare in bradycardia in this instance it is due perhaps to the increased filling of the heart during prolonged diastole

Fatigue In advanced mitral stenosis fatigue is often an outstanding symptom The marked reduction of cardiac output is presumably responsible The cardiac output per minute may fall to 2 liters

Anginal Pain A small percentage of patients with mitral stenosis complain of anginal pain which often appears at rest and occasionally is not relieved by nitroglycerin Stuckey found pain in 8 5 per cent of 400 patients with mitral stenosis Scherf and Goldhammer found a positive electrocardiographic exercise test in such patients proving that cardiac hypoxia was responsible in the patients examined Compression of the left coronary artery between the left atrium and pulmonary artery or displacement and compression of the left coronary orifice by scars in the mitral valves have been proferred as explanations but they lack satisfactory proof The intermittent claudication occasionally observed in mitral stenosis in the absence of peripheral vascular disease shows that a diminished minute volume may be responsible

Signs

Complexion Sometimes inspection reveals the typical mitral facies with the malar flush and cyanotic tint of the lips and ear lobes Often however patients look normal Cyanosis in mitral stenosis is caused by pulmonary congestion by pulmonary vascular sclerosis in later stages or by increased peripheral utilization of the blood oxygen and stagnation in the advanced stage with right heart failure

Therefore cyanosis may be absent early unless pulmonary congestion is present It may diminish or disappear after having been present if the liver enlarges moderately and venous congestion develops due to right heart failure

Pulse Palpation of the pulse has considerable importance in the appraisal of this valvular lesion In advanced mitral stenosis filling of the left ventricle in diastole becomes so reduced that the stroke volume is diminished and the pulse is very small it may be scarcely palpable at the wrist even if it is felt in the larger carotid arteries If the patient has only a slight stenosis of the valve the pulse is normal One may infer therefore to a certain degree the amount of stenosis from the amplitude of the pulse In a beginning stenosis the pulse is normal but it becomes smaller as the stenosis increases Other physical signs are less informative in regard to the degree of stenosis than the pulse Thus murmurs may be both absent when the stenosis is advanced and very loud in the initial phase of the disease

Mitral stenosis and mitral insufficiency are often combined Under these circumstances the pulse alone reveals which lesion predominates As will be noted later mitral regurgitation does not decrease the size of the pulse Therefore if the pulse is normal in a combined mitral lesion it may be assumed that the stenosis is not extreme A small pulse in such cases indicates an advanced stenosis

even when the murmur of stenosis is absent and the murmur of mitral insufficiency is very loud

The pulse is also poorly filled and small in stenosis of the aortic valves in myocardial weakness and in the shock syndrome but the differentiation usually is easy

Blood Pressure In a youthful patient with mitral stenosis the blood pressure tends to be lower than the average level for the same age in the general population With increasing age (or with the appearance of decompensation) the blood pressure often rises and sometimes reaches a high level Some believe that the incidence of hypertension in mitral stenosis is the same as in the general population

Palpation Examination of the thorax and especially of the precordium by palpation in mitral stenosis yields so many signs that this method of investigation permits the diagnosis in most cases The apical impulse often remains at its normal site This might be anticipated since the left ventricle does not assume the burden of compensation and does not enlarge The right ventricle dilates only at a later stage and at this time the apex beat may be felt lateral to but never below its normal location If the apex beat is displaced downward the left ventricle is dilated and some complication such as mitral or aortic insufficiency exists and has produced the left ventricular enlargement

The apical impulse is abnormal in another respect It becomes snappy and quicker than normal In a normal heart if the apex can be felt at all it gives the impression of a slow pulsation In left ventricular hypertrophy it is heaving and particularly slow In a mitral stenosis however it is very short This alteration of the apex beat corresponds to the accentuation of the first heart sound a very common finding in mitral stenosis and enables one to make the correct diagnosis in the numerous instances when murmurs are absent

In an advanced mitral stenosis the left ventricle is smaller than normal sometimes it is even atrophic While it normally constitutes the most massive section of the heart in advanced mitral stenosis the left ventricle often looks like an appendage to the rest of the organ The left atrium right atrium and right ventricle hypertrophy and dilate in the evolution of the lesion but the left *ventricle does not participate* in the compensation *The atrophy is usually attributed* to the inadequate filling of the left ventricle and the fact that it involves the inflow tract primarily suggests that this assumption is correct

Another reason for the atrophy of the left ventricle also deserves consideration During the last years of life patients with advanced mitral stenosis are compelled to avoid the least exertion because this provokes dyspnea Such enforced inactivity which results in considerable atrophy of the skeletal musculature attains very striking proportions in mitral stenosis There is a strict parallelism between the status of the skeletal muscles and the state of the left ventricle In muscular athletes the left ventricle is stronger and heavier than in the average person in sedentary individuals who are physically inactive the left ventricle is weaker and less capable of performance Probably part of the left ventricular atrophy in cases of advanced mitral stenosis is due to inactivity of the patient

This fact should make one hesitate to limit the activity too strictly in patients with valvular lesions *All physical exertion should not be forbidden The patient* should be permitted to do as much physical work (initially under supervision) as he can without symptoms Like every other muscle the heart must also do its share of work in order to retain as much functional capacity as possible

A diastolic thrill is often palpable in the apical area A diastolic thrill means a diastolic murmur the significance of this lies in the fact that diastolic murmurs are found only in organic heart disease Systolic thrills which accompany systolic murmurs occasionally may be devoid of significance when the murmur is functional or physiologic The thrill of mitral stenosis appears more often if the apical area is palpated with the patient lying on his left side Its diastolic character is easily determined when the carotid pulse is palpated simultaneously and it is found that *one does not coincide with the other*

The regularity with which the murmur of mitral stenosis is accompanied by a *thrill* is explained by the fact that the murmur is *low* in pitch and the chest is resonant to low pitched murmurs Vocal fremitus is scarcely palpable in individuals with high pitched voices (mostly women) while it may be very distinct in men with deep voices (chest voice) This accounts for the usual absence of thrills in insufficiency of the aortic valve with its soft high pitched murmur The murmurs in all stenotic mechanisms of organic heart disease are low pitched and cause thrills This is also exemplified by the murmurs in aortic stenosis and in congenital cardiovascular defects

Occasionally the murmurs are so low pitched and have such coarse vibrations *of large amplitude that they can be better palpated than heard The human ear* is unable to perceive murmurs with less than sixteen vibrations per second *Thus it occasionally happens that a patient with mitral stenosis presents a distinct* thrill yet the murmur is very short or even inaudible

Palpation also reveals the signs of right ventricular hypertrophy that is a diffuse pulsation over the entire precordium Since the outflow tract of the right ventricle bears the chief burden of compensation and the conus of the right ventricle projects as the most ventral part of the heart systolic pulsation in the conus area may be pronounced Furthermore a brief but distinct impact is often felt in the conus area along the left cardiac border This impact follows the slow systolic pulsation over the precordial area and does not coincide with the carotid pulse It corresponds to the closure of the pulmonic valve which produces the second pulmonic sound The second pulmonic sound is normally palpable over the area of the pulmonary conus only in early childhood In adults palpability of the pulmonic sound is just as significant as the marked accentuation that always accompanies it Occasionally the closure of the pulmonic valve is palpable only during expiration

The wealth of manifestations on palpation — the *snappy apical impulse* the diastolic thrill at the apex the diffuse pulsation over the precordium and the *more circumscribed systolic movement over the conus area of the right ventricle* the distinctly palpable closure of the pulmonic valve — all these signs permit

the immediate diagnosis of mitral stenosis in a majority of cases By palpation of the pulse one can determine the extent of the lesion

To be sure even moderate emphysema makes the detection of these phenomena *difficult or impossible Moreover some of the above mentioned* phenomena occur in the absence of mitral stenosis Thus in the hyperactive heart of hyperthyroidism and of many patients with cardiac neuroses in some cases of beriberi or hypertension a diffuse precordial pulsation may be found in the absence of right ventricular hypertrophy In hyperthyroidism and cardiac neurosis the apex beat may be snappy and even preceded by a very short thrill By considering the other physical findings however a differentiation is usually easy

Percussion and Roentgen Examination

The size and shape of the heart in mitral stenosis may reveal three different situations which like the three cardiac contours seen in aortic insufficiency correspond to three sequential stages of the lesion Such findings are (1) a heart of normal size and shape (2) a mitralized heart of normal size (3) an enlarged mitral heart

(1) *For many years in cases of mitral stenosis the heart may* be perfectly normal in size and shape despite the presence of a loud presystolic murmur For obvious reasons this event is rare in clinics and in hospital wards but it is not uncommon in private practice One of us collected within one year 16 cases of mitral stenosis which did not present changes in the contour or size of the heart This situation prevails as long as the left atrium by hypertrophy alone is able to force sufficient blood into the left ventricle Under these circumstances no stasis develops no visible enlargement of the left atrium appears and the cardiac shape is normal Left atrial hypertrophy cannot be percussed and is not visualized by x ray *examination Sometimes the heart retains its normal shape* even if the auscultatory and roentgenologic findings indicate some congestion in the lesser circuit and the right ventricle becomes hypertrophic Therefore mitral stenosis should not be excluded in doubtful cases on the basis of normal x ray findings The heart may be normal in size even with the presence of a tight mitral lesion

(2) When left atrial hypertrophy no longer successfully maintains compensation increasingly larger residues of blood remain in the left atrium at the end of systole and dilatation develops The elevated pressure in the left atrium leads to a *similar increase within the pulmonary veins and soon—in a manner not completely* clear — in the arterial segment of the lesser circulation The elastic wall of the pulmonary artery expands The increased work for the right ventricle leads to a hypertrophy and dilatation of the outflow tract the conus area

The dilatation of the outflow tract of the right ventricle as pointed out before develops cephalad This change occasionally combined with dilatation of the left atrium causes the normal waistline on the left cardiac border to disappear and mitral configuration is found (figure 29 a)

A third mechanism is considered an important factor in the disappearance of the cardiac waist particularly in the late stages of mitral stenosis Dilatation of the right ventricle causes the heart to rotate around its axis to the left This rotation around the cardiac axis is clockwise (if the examiner stands opposite the patient) and is due mainly to an *enlargement of the outflow tract of the right ventricle* which lying anteriorly with an almost perpendicular axis fills the waistline if it becomes dilated Enlargement of the inflow tract counteracts this rotation and may even nullify it In a similar manner the heart rotates to

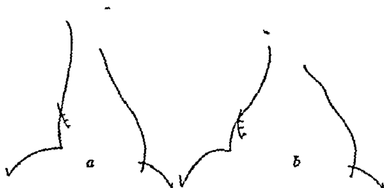


FIG 29 Two orthodiagrams obtained from patients with mitral stenosis (a) Mitral configuration with moderate dilatation in the transverse diameter (b) Marked dilatation *of the heart to the right and left In both instances the left atrium is visible on the right side*

the right (counter clockwise) *with dilatation of the outflow tract of the left* ventricle dilatation of the inflow tract of the left ventricle again opposes this rotation Thus it happens that the right ventricle not only fills the waistline progressively but forms the main part of the left cardiac border down to and including the apical area Instead of the normal concavity the left heart border appears convex with the lower part of the left border extending *almost perpendicularly* toward the apex which is situated at its normal place (figure 30) This form of the heart is so *characteristic that* one may speak of a mitral stenosis configuration (Holzmann)

Although the left atrium normally is situated posteriorly it becomes visible at the right border of the heart in about 50 per cent of the cases with mitral stenosis this is due to rotation of the heart and to enlargement of the left atrium *Sometimes the left atrium bulges far into the right lung field and a double contour* is formed due to the superimposition of the right and left atrium (figure 29) The left atrium may be visible at the right *and* the left cardiac border (figure 31)

If the left lower heart border runs obliquely to the left the mitral stenosis is combined with some lesion which causes an enlargement of the left ventricle Usually this will be a mitral insufficiency but occasionally an aortic insufficiency or hypertension will be responsible



FIG 30 Mitral stenosis configuration in a patient with rheumatic mitral stenosis



FIG 31 Giant left atrium in a patient with rheumatic mitral stenosis The left atrium forms a great part of the left and right cardiac border The lung fields are clear

The huge proportions of the atrium in some cases of mitral stenosis are remarkable One case is known in which it had a capacity of three liters (Minkowski) An enormously dilated atrium may fill the right chest and may be confused with a right sided pleural effusion Even moderate dilatation of the left atrium can produce left paravertebral dullness between the third and eighth dorsal vertebra It may erode the vertebrae It should be stressed however that a very large left atrium is encountered more often in mitral regurgitation than in stenosis An unusual degree of dilatation which at times is encountered even with a slight mitral stenosis is clearly not due to dynamic factors alone An old carditis with fibrosis of the atrial wall plays an important part

A markedly dilated left atrium forms a large blood depot and acts like an enlarged liver in diminishing pulmonary congestion and dyspnea even in an advanced stenosis

Due to the rotation of the heart and the diminishing output the aortic knob tends to disappear in the mitral heart this happens especially when the mitral stenosis is acquired in early childhood The dilated pulmonary artery and conus also push back the aorta (Zdansky)

The increased pressure within the lesser circuit causes the hilar markings to enlarge but they are sharply outlined Pulsations are strong and may equal those observed in the 'hilar dance' seen in defects of the ventricular septum pulmonary regurgitation persistent ductus arteriosus fever and hyperthyroidism

(3) Marked dilatation of the inflow tract of the right ventricle finally develops The apical impulse becomes palpable beyond the midclavicular line and the cardiac shadow enlarges to the left and to the right (figure 29 b) dilatation of the right atrium causes a distinct dullness to the right of the lower sternum

If the myocardium is damaged this third stage is reached even before the valvular lesion becomes very advanced with a normal myocardium however this stage appears late

Auscultation

Auscultation reveals a very loud accentuated sometimes tympanitic or bell like first heart sound in the region of the apex There are two reasons for this accentuation (1) the mitral valves are changed by increased amounts of connective tissue and lime salt deposits (2) the filling of the left ventricle is diminished

Vibrations due to the valvular closure and systole are apparently intensified if the filling of the ventricle is diminished empty barrels make the most noise Actually a very loud first heart sound is heard during syncope and sometimes in shock when the content of the left ventricle diminishes A loud first sound is heard when the heart is overactive as in hyperthyroidism or cardiac neurosis This occurs not only as the result of hyperactivity but also because the tachycardia regularly present in these conditions shortens diastole and diminishes ventricular filling A loud first heart sound is also noted in extrasystoles when the premature contraction occurs very early in diastole

Another explanation of the sharp first sound is the abrupt intra-atrial displacement of the leaflets which have decreased length and mass (Nichols et al)

The accentuation of the first heart sound will be absent when the left ventricle fills sufficiently due to an accompanying mitral or aortic insufficiency It is also absent when the valves are calcified and not flexible The change of the first heart sound is rarely the sole basis for the diagnosis of mitral stenosis Often however it is a finding leading to a careful examination which will reveal the diagnosis

In the phonocardiogram a delay of the appearance of the vibrations of the first heart sound is found (Cossio and Berconsky) Instead of appearing about 0 04 second after the beginning of the QRS complex in the electrocardiogram they appear after an interval of 0 08 second or more (figure 33 a)

In very early mitral stenosis murmurs may be absent and pure sounds are heard The valvular alterations are too trivial to create abnormal eddies and murmurs Nevertheless a murmur may appear in these cases if the examination is conducted immediately after exertion or after the inhalation of amyl nitrite (Morrison test)

Generally speaking a murmur may appear or may become louder *first* if the stenosis becomes greater (this cannot be produced artificially) or second if the velocity of blood flow is accelerated by exercise or amyl nitrite

The murmur appears first at the end of diastole that is in the presystolic period This presystolic murmur seems to begin softly then gradually become louder ending in the accentuated first heart sound (figure 32 a) It is called the presystolic crescendo murmur Actually graphic records reveal that this murmur is often continuously of the same intensity the crescendo character is often an auditory impression due to the sound immediately following the murmur (Lewis)

The ventricle is filled from the atrium chiefly during the initial phases of diastole Therefore it is striking that the murmur of mitral stenosis is often heard only at the end of the diastole presystolic rather than at the beginning The reason is as follows filling of the ventricles in the beginning of diastole depends mainly upon the influx of blood when pressure in the atrium and ventricle differ Late in ventricular diastole however the atrium contracts increasing the speed of flow enough to produce a murmur in the case of a slight mitral stenosis Thus in this instance as well as in many others the velocity of blood flow is responsible for the development of a murmur

If the stenosis of the mitral valve progresses the inflow *of blood in the* earlier phases of diastole also produces a murmur and this is truly decrescendo it is loud at first since intra atrial pressure is higher at the beginning of diastole and the blood flows speedily into the ventricle Later in diastole atrial pressure diminishes and the murmur becomes softer It often vanishes momentarily until the atrial contraction causes the presystolic murmur to occur Occasionally one murmur merges directly into the other especially when the rate is fast so that all diastole is occupied by the characteristic rumble In this stage one

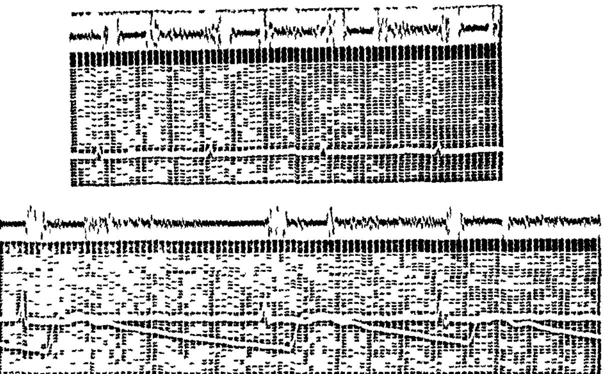


Fig. 3. (a) Mitral stenosis with sinus rhythm. Stethogram from apical area, with a crescendo presystolic and a diastolic murmur. A faint systolic murmur indicated the presence of a mitral regurgitation. (b) Mitral stenosis and atrial fibrillation: at the apical area a prolonged diastolic murmur was audible in addition to a soft systolic murmur.

hears the classic *ffout tataran* of Duroziez which is more closely approximated by *rrt tataran*

Thus an increase in the degree of mitral stenosis may intensify the murmur in certain stages At the beginning of a mitral stenosis all murmurs may be absent during rest Later a presystolic rumble is audible and finally a murmur appears in the early part of diastole as well At any time however the common complications of mitral stenosis to be discussed presently may develop and the murmurs disappear Therefore patients with loud murmurs are encountered more often in private practice and in out patient clinics among the ambulatory group than in those confined to hospital wards

The first murmur to vanish the murmur which disappears sooner or later in the course of every mitral stenosis is the presystolic murmur Since it develops from an accelerated inflow of blood produced by atrial systole it vanishes when the left atrium ceases to contract normally There are two reasons for this disappearance

(1) Marked overdistention of the left atrium makes the presystolic murmur vanish The ventricles are composed chiefly of muscle fibers with a few interspersed connective tissue and elastic fibers the atria however are formed by a network of small muscle bundles the meshes of which are filled with considerable fat and connective tissue Pronounced dilatation of the left atrium soon overstretches these bundles and reduces their contractile power From the standpoint of cardiac dynamics overdilatation of the atrium means paralysis of this chamber Such an atrium acts chiefly as a reservoir and does not assist in the propulsion of blood Thus with progressive dilatation of the left atrium the presystolic murmur becomes ever shorter until it vanishes completely If a loud drawn out presystolic murmur is still audible certainly the left atrium is not markedly dilated and is able to perform valuable work in compensating the valvular lesion If on the other hand a case of mitral stenosis with regular cardiac action comes under observation and no presystolic murmur is detected it is justifiable to infer the presence of marked left atrial dilatation from this finding alone Usually this is confirmed by fluoroscopy

(2) The second cause for the disappearance of the presystolic murmur is atrial fibrillation (figure 32 b) In fibrillation so many stimuli are formed in the atrium (approximately 600 per minute) that coordinated contraction ceases The atria show very rapid scarcely visible remarkably feeble movements and therefore as far as the dynamics are concerned one may speak of a paralysis of the atria With the onset of fibrillation the presystolic murmur vanishes This event occurs sooner or later in most cases of mitral stenosis

The murmur that appears in early diastole does not owe its development to the atrial contraction and therefore remains during atrial fibrillation just as it persists when the left atrium is greatly dilated In some cases however the presystolic murmur disappears at a time when no diastolic murmur was present In this instance the lesion becomes mute or silent

Since ventricular rhythm is completely irregular in atrial fibrillation and repeatedly one beat follows another after a very short diastole the diastolic murmur may appear just before the first heart sound of the following beat in this case it may seem to develop a crescendo character and may simulate a presystolic murmur This explains the recurrent but erroneous report that presystolic murmurs are heard in spite of fibrillation If such patients are digitalized and diastole is lengthened by slowing of the rate one can readily be convinced that the murmur is purely diastolic (figure 32 b)

Some believe that the presystolic murmur of mitral stenosis originates not from the atrial contraction but rather from ventricular activity and that it is a systolic phenomenon Graphic registration and the observation of the same presystolic murmur in 2 1 atrioventricular block even during the atrial systole which is not followed by a ventricular contraction prove that the murmur is actually caused by the atrial contraction

The silent (mute) type of mitral stenosis is not limited to early cases nor to those cases in which the presystolic murmur disappears before the diastolic murmur has appeared The diastolic murmur may also vanish as the lesion progresses if the valvular ring becomes rigid calcified and narrower (tight mitral stenosis) The flow of blood into the ventricle becomes progressively slower until the blood merely trickles into the chamber when the velocity of blood flow diminishes enough the murmur disappears

Under all these circumstances the lesion must be recognized by other signs by palpation and percussion in particular The silent type of mitral stenosis is not rare and probably about 50 per cent of the cases observed for a sufficiently long time are temporarily silent The characteristic history of increasing exertional dyspnea in the absence of nocturnal dyspnea facilitates the diagnosis

Too often however the lesion is considered silent even though murmurs are present for the murmurs are not detected when certain rules are disregarded These rules should be followed diligently in the auscultation of these cases

The murmurs of mitral stenosis almost without exception are not widely transmitted While other murmurs even if moderately loud are heard in several places or even over the entire heart the murmurs of mitral stenosis are audible only in circumscribed areas They vanish if the stethoscope is shifted only a little For this reason the apical area must be examined very carefully point by point when mitral stenosis is suspected Most frequently the murmur if present is found at the area of the apical impulse Occasionally it is heard outside of the apex beat nearer to the axillary line and in rare cases inside nearer the left sternal border In mitral stenosis only relatively slight differences in pressure within the cardiac chambers are involved the murmurs are therefore never exceedingly loud

Very often the murmur like the thrill is perceptible only when the patient assumes the left lateral position Auscultation in this position should never be omitted when mitral stenosis is suspected and no murmurs are heard in the supine posture The murmurs of mitral stenosis are also often overlooked when patients

are examined while they are standing For this reason instances of mitral stenosis are often missed in school examinations and other routine health surveys in which the examining physician listens to the heart only while the patient is in the erect posture

Another reason for missing the murmurs of mitral stenosis is that they present peculiar qualities Owing to their low pitch these murmurs sound quite different from other murmurs The murmurs are rough uneven and give the impression of a short rumble or a few split sounds rather than of gushing and flowing of liquid in the manner of other murmurs If the murmur is very brief it is particularly difficult to differentiate from an impure sound Thus students frequently report having heard no murmur in a given case — until they learn that the rough rumble they noted was the characteristic murmur of mitral stenosis Undoubtedly some experience is necessary in order to recognize this particular diastolic murmur

In some cases the diastolic murmur of mitral stenosis must be distinguished from a diastolic murmur of aortic insufficiency As has been pointed out both murmurs may be heard at the apical area Quite often in pulmonary emphysema for example it is audible only at this place The physical findings in a pure aortic insufficiency to be sure differ vastly from those in a pure mitral stenosis At the beginning however and before characteristic physical signs develop or when mitral and aortic valve involvement are combined it is not always easy to decide whether the apical diastolic murmur is due to mitral stenosis or aortic insufficiency The low pitched rumble of mitral stenosis is not always sufficiently pronounced to permit differentiation

In an insufficiency of the aortic valve the diastolic murmur immediately follows the second sound since high intra aortic pressure causes an immediate regurgitation of blood into the left ventricle through the incompetent valve In a mitral stenosis the diastolic flow of blood from the left atrium into the ventricle encounters an obstruction resulting in a diastolic murmur The left atrial pressure however is considerably lower than the intra aortic pressure Until the mitral valve opens and the pressure in the ventricle is sufficiently low to permit the blood to flow from the atrium to the ventricle an interval elapses Hence the murmur of mitral stenosis does not follow the second sound immediately as in the case of aortic insufficiency it appears after an easily perceptible interval which separates it from the second sound While a bipartite rhythm (to and fro murmur) is heard in aortic insufficiency it is tripartite in mitral stenosis In the latter one hears the loud first sound (and a systolic murmur since a mitral insufficiency often coexists) then the second sound and finally after a short pause there is the diastolic murmur of mitral stenosis This triple event closely resembles gallop rhythm particularly when the diastolic murmur is very short and rough and thus difficult to differentiate from a heart sound

The second pulmonic sound is often accentuated Increased pressure within the lesser circuit is advanced as the primary factor in the accentuation since this causes more forcible closure of the valves There is however another very important mechanism dilatation of the conus of the right ventricle and of the

pulmonary artery brings these structures nearer to the thoracic wall so that the second sound is conducted better to our ear Just as a dilated ascending aorta transmits the diastolic murmur of aortic insufficiency better to the second right intercostal space so the dilated pulmonary artery and pulmonary conus conduct the second pulmonic sound better to the left Actually this accentuation is not heard best nor is the shock due to the closure of the pulmonic valves felt best in the area of the actual location of the valves rather one hears and feels the second pulmonic sound where the wall of the conus or pulmonary artery comes in contact with the thoracic wall This is usually in the second or third interspace along the left cardiac border

An accentuated second pulmonic sound is not invariably found in mitral stenosis As long as the pressure within the lesser circuit is not elevated — as long as the left atrium compensates the stenosis perfectly — the second pulmonic sound is normal A previously existing accentuation may disappear if the pressure in the lesser circuit falls owing to the appearance of right ventricular failure On the other hand young individuals occasionally up to the age of twenty five often show a distinct accentuation of the second pulmonic sound in the absence of a mitral lesion In youth the pulmonary artery physiologically is wide and prominent it lies near to the thoracic wall so that the second pulmonic sound is louder than the second aortic sound Beyond the age of thirty five the second aortic sound normally becomes slightly louder

These facts indicate that the importance of an accentuated second pulmonic sound in the diagnosis of a mitral lesion has been overrated in the past

Apart from an accentuation a splitting (duplication) of the second pulmonic sound is found This phenomenon is also observed in healthy young people Although a final explanation is not as yet available many believe that the duplication is due to an asynchronous closure of the aortic and pulmonic valves This explanation seems logical since in mitral lesions the increased pressure in the lesser circuit should cause the pulmonic valves to close earlier Normally both shut at the same time despite the fact that the aortic pressure is approximately six times as high as the pulmonic pressure If this explanation were exclusively valid the duplication should be heard distinctly over the aorta as well whereas it is actually found only over the pulmonic area Therefore it is possible that the individual pulmonic valves themselves do not close simultaneously The dilated conus of the pulmonary artery with its ostium thrust forward by the dilated left atrium might be partly compressed by the anterior chest wall so that the three pulmonary valves no longer lie in the same plane and no longer close simultaneously Against this explanation is the fact that very slight differences are involved which are scarcely perceptible to the human ear However not rarely the duplicated second sound is palpable in the form of a short circumscribed double shock exactly over the pulmonary area that is at the place where it may arise

The *opening snap* (claquement d ouverture de la mitrale opening click) is a phenomenon which is heard in a majority of patients with mitral stenosis

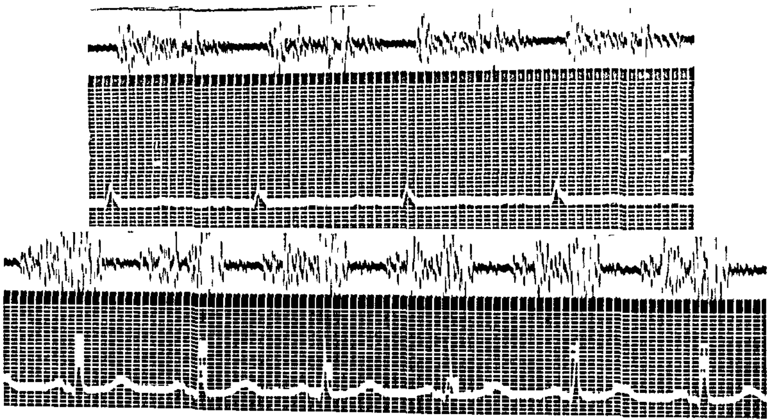


FIG 33 (a) Mitral stenosis and regurgitation with sinus rhythm There is a systolic and diastolic murmur with an opening snap (b) Tracing obtained from a 38 year old woman with rheumatic mitral stenosis there is a soft systolic apical murmur and a rumbling diastolic one with an opening snap of the mitral valve

(figure 33) It is a short high pitched sound which appears in the phonocardiogram 0 09 to 0 13 second after the beginning of the second heart sound It coincides with the peak of the V wave in the phlebogram Others claiming that this interval should be shorter than 0 08 second speak of a third heart sound when it amounts to 0 12 second or more (Ongley et al) It is rarely found over the whole heart usually appearing on the left lower sternal border or about halfway between the apex and left sternal border It is also present in atrial fibrillation It is absent in patients with a very mild stenosis of the valves and when the valves are markedly calcified It is also absent when mitral regurgitation predominates These facts have great importance in the evaluation of a patient for surgery The opening snap is heard best with the patient in the supine position The diastolic murmur is separated from the opening snap by a very short interval Often the snap is hidden from our ears in the murmur Its relation to the second sound varies with the length of the preceding diastole If this is short the closure of the mitral valve is delayed and the time interval between the second sound and the snap is shorter The distance between the second heart sound and the snap depends on the height of left atrial pressure The phenomenon is explained by the sudden tension of the fused mitral valves at the beginning of diastole when the downward movement of the valves is suddenly inhibited

It is higher in pitch and shorter in duration than the second sound or the third heart sound Monsey found an opening snap on 28 of 33 patients with mitral stenosis

Systolic Pulmonary Murmurs Not rarely these patients exhibit a systolic murmur at the pulmonic area Occasionally this murmur may be very loud and rough it may even be associated with a thrill and may dominate the auscultatory picture As a cause of this murmur the previously mentioned compression of the pulmonary artery by the anterior chest wall has been advanced (functional supravalvular pulmonary stenosis) Another and in our opinion better explanation is based upon the fact that in mitral stenosis both the right ventricle and pulmonary artery are dilated so that the valve ring whose diameter is normal acts as a relative stenosis

Diastolic Pulmonary Murmurs Occasionally there is a high pitched diastolic murmur to the left of the sternum in the fourth or fifth interspace this is due to a relative pulmonary insufficiency The murmur and its mechanism will be discussed later

Angiocardiography

Angiocardiography has been recommended as a diagnostic method for the selection of patients for surgery In advanced mitral stenosis prolonged and dense opacities are found in the left atrium while the left ventricle is not opacified to the same degree

Electrocardiography

This may aid in diagnosis The P waves are often abnormally wide (more than 0 12 second) and they are slurred in leads I and II (figure 8 a) There is often a right axis deviation and in more advanced cases evidence of right ventricular hypertrophy (the PS—T segments and T waves are directed opposite to the main deflection) (figure 13) The R waves in V2 are often higher the S waves in V5 and V6 deeper than normal The T waves in V2 and V3 are often inverted When the left ventricle is also affected due to a mitral insufficiency aortic insufficiency left axis deviation or no axis deviation is found In such cases the P waves changes alone are significant Atrial fibrillation is common

Differential Diagnosis

The low pitch of the murmurs in mitral stenosis makes them sound very much like an impure or split heart sound — a common source of error

Experience shows that physicians who become interested in heart diseases for some time make the diagnosis of mitral stenosis too often because they diagnose the lesion in every case exhibiting an impurity of the first heart sound at the apex A presystolic murmur is believed to be present when the first heart sound is split especially when the vibrations of the first part are softer than those of the rest of the first heart sound Splitting of the first heart sound often depends upon an audibility of the atrial sound this is a common event in the hyperexcitable heart of hyperthyroidism and cardiac neurosis It is not rare in an advanced anemia and was common when the treatment of pernicious anemia was restricted to arsenicals and iron Duplication of the first sound also occurs in kyphoscoliosis and pleural adhesions Since the first heart sound is abnormally loud in most of the aforementioned conditions confusion with mitral stenosis is possible Splitting of the first heart sound at the apical area also appears in some congenital heart lesions (patent ductus arteriosus atrial septal defect) as well as in hypertension and coronary sclerosis To be sure these cases lack the long drawn out presystolic rumble and present only a brief impure sound be fore the first heart sound but the same acoustic phenomenon is also found in mitral stenosis

The Austin Flint murmur wrongly believed by many to be common has been discussed above It may be either presystolic or early diastolic Since the left atrium is dilated in these cases and the second pulmonic sound may be accentu ated distinction from an actual mitral stenosis is often impossible during life

Diastolic murmurs of the same origin have been described in patent ductus arteriosus and in atrial septal defects In the latter this murmur leads to the wrong diagnosis of Lutembacher s syndrome It has also been observed in active rheumatic fever It is explained by the whirlpools created by the inflow of blood into the dilated left ventricle

Occasionally the acoustic phenomena caused by the atrial contraction in partial atrioventricular block are confused with the murmurs of mitral stenosis

A mid diastolic rumble like that of mitral stenosis is present in many cases of 2 1 block The sound caused by the atrial contraction is often double or split This produces the very close resemblance to a diastolic rumbling mitral murmur

The clinical picture of mitral stenosis is imitated by myxoma of the atria, particularly the left one With angiocardiography the diagnosis is possible during life because of the constant presence of a filling defect in the atrium (Steinberg et al)

These imitations of the murmurs of mitral stenosis as well as the fact that real organic mitral stenosis often presents no murmurs for some time make the diagnosis of some cases of mitral stenosis more difficult than is commonly realized

Complications

Atrial Fibrillation This is one of the most common complications in the course of mitral stenosis It is usually present in the more advanced cases on the hospital ward but it may appear at any time even in the very early stages of the lesion

The disturbance of the circulation due to atrial fibrillation will be discussed in a later chapter In regard to mitral stenosis the increased rate so often appearing at the onset of fibrillation and the disappearance of effective contractions of the left atrium are harmful Many cases of mitral stenosis begin to show evidence of decompensation with the onset of atrial fibrillation

The fact should be stressed however that atrial fibrillation proves a useful complication in other cases of mitral stenosis and may serve to make life more tolerable and even to prolong it As long as sinus rhythm prevails in a compensated mitral stenosis the rate is often very high and may reach 120 beats per minute Since a longer diastole is necessary in mitral stenosis to permit blood to pass through the stenotic valve this tachycardia serves to increase congestion within the left atrium and the lesser circuit Digitalis does not slow such hearts in fact there is no beneficial treatment available for these patients except mercurial diuretics which somewhat diminish the fluid content of the lungs and relieve dyspnea and orthopnea In such cases the appearance of atrial fibrillation affords great relief It is true that the fibrillating atrium is unable to contract effectively and cannot help compensate the lesion this fact is of no consequence however because the left atrium is usually overdilated in the first place and therefore without significance from the standpoint of dynamics In fibrillation with mitral stenosis digitalis can slow the heart to such a degree that the length of diastole almost doubles Therefore pulmonary congestion quickly diminishes and patients may live comfortably for years

Undoubtedly many patients live to reach the button hole stage of mitral stenosis only because atrial fibrillation occurred

Before atrial fibrillation is established patients sometimes pass through a stage of paroxysmal fibrillation in which the attacks last a few minutes hours or days In this instance treatment may be difficult because the attacks do not

recur sufficiently often for preventive treatment with quinidine nor do they last long enough to permit the use of digitalis With a longer duration of the attacks of paroxysmal fibrillation and when the physician has the impression that the patient would be better off with sinus rhythm 0 20 Gm quinidine sulphate is given every two hours until the attack subsides But when atrial fibrillation has been definitely established in cases of mitral stenosis there is rarely an indication for abolishing it by quinidine

Mural Thrombi and Embolism Not uncommonly mural thrombi form in the dilated left atrium especially if atrial fibrillation is present They are not the result of a stagnant circulation alone but are usually due to involvement of the atrial endocardium by the rheumatic process this often causes deposits of fibrin as well as the formation of thrombi at the affected area

Detached fragments of such thrombi may produce vascular accidents such as cerebral embolism or embolism in a peripheral artery The middle cerebral artery is often affected by such emboli In a series of 72 cases of mitral stenosis with cerebral embolism atrial fibrillation was present in 55 (Harris and Levine) Recovery from a cerebral embolism sometimes progresses with astonishing speed and to a surprising extent

It has been established that peripheral embolism occurs in 5 to 10 per cent of cases of mitral stenosis After the first embolism occurs the physician is confronted with the problem whether to use prophylactic therapy with anticoagulants Because of the necessity to maintain a certain critical prothrombin level the dangers of such therapy and the rarity of recurrences this treatment is utilized only for special patients exhibiting frequent embolic manifestations Embolism occurs in spite of correctly guided therapy with anticoagulants

Tuberculosis The frequently encountered statement that pulmonary congestion in mitral stenosis protects the patients from pulmonary tuberculosis is not justified It seems that pulmonary tuberculosis in patients with mitral stenosis is as common as in the general population

Pulmonary Hemoptysis This complication has various causes It may appear in pulmonary embolism with infarction it is seen in acute pulmonary congestion or in pulmonary edema It is observed even in the presence of atrial fibrillation Sometimes amounts up to 500 ml of blood are expectorated at one time A leukocytosis and mild fever may be present The patient may complain of precordial distress The lung fields show mottling roentgenologically A rupture of pulmonary veins or varices of the bronchial veins may be responsible

Ball Thrombus A rather rare and interesting complication is a ball thrombus in the left or rarely right atrium This thrombus may be sufficiently large to fill the entire atrium The true ball thrombus is free or may be attached to the atrial wall by a pedicle Atrial fibrillation is usually present The clinical diagnosis of this complication sometimes is possible since the thrombus very markedly disturbs the circulation and causes certain characteristic signs Angiocardiography demonstrating a filling defect in the atrium may help These patients usually have deep cyano is and severe dyspnea the peripheral parts of the body

especially the feet and legs are cold the peripheral pulses are almost impercep tible and gangrene develops in the toes fingers nose and ears This gangrene is often symmetrical because the minute volume undergoes extreme reduction due to the obstruction of the mitral orifice It would be asymmetric if the gangrene were the result of embolism which sometimes appears in the peripheral arteries The evolution of symptoms from the initial coldness of the extremities to pallor lividity necrosis and gangrene may require weeks

In addition to these permanent features transient complications may follow temporary impaction of the ball thrombus in the mitral orifice Such patients have attacks of fainting and disturbances of speech or paralysis of the limbs Disorientation and convulsive seizures occur if the impaction lasts longer Natu rally prolonged block of the mitral orifice is fatal

In one of our cases (Lans) with the picture just described large thrombi practically filled the whole atrium and obstructed the orifices of the pulmonic veins to a great degree The presence of a ball thrombus is thus not necessary for this clinical syndrome to appear

Obviously the prognosis of these patients is poor A duration of life exceed ing one month after the appearance of symptoms is apparently rare Atrial fibrillation in the absence of mitral stenosis is rarely associated with the forma tion of a ball thrombus but such cases have been observed in hypertension We saw a somewhat similar syndrome as a consequence of a ball thrombus in the right atrium Surgery for removal of the thrombus should be contemplated

A similar picture may be found in atrial myxoma where the glossy gelatinous tumor may fill the whole left atrium These tumors histologically have a structure like Wharton s jelly of the umbilical cord They appear in hearts without mitral stenosis and represent the most common primary new growth of the heart

Laryngeal Nerve Paralysis A paralysis of the left recurrent laryngeal nerve causing hoarseness sometimes occurs Originally this phenomenon was explained by a compression of the nerve between the enlarged left atrium and the arch of the aorta It seems however that the nerve is squeezed between the aorta and left pulmonary artery when the latter is pushed forward by the enlarged left atrium

Paralysis of the left recurrent laryngeal nerve due to a similar mechanism has also been described in connection with left ventricular failure (King et al) Improvement has been observed following mitral surgery (Ari et al)

Dysphagia This is an occasional result of the marked dilatation of the left atrium Posterior displacement of the esophagus is usually accompanied by a lateral displacement (in most cases to the right) so that the esophagus usually but not invariably escapes compression

Dysphagia also occurs in pericarditis with effusion in rare cases of left ventricular enlargement (aortic stenosis) in anomalies of the aortic arch and of the large arteries originating from the aorta (dysphagia lusoria) and saccular as well as dissecting aneurysms the three conditions mentioned last are provocative most often

Bronchial Stenosis Since the left atrium is situated just beneath the tracheal bifurcation atrial enlargement may increase the angle of the bifurcation The angle of the two main bronchi is normally about 70 degrees and always less than 90 degrees In mitral stenosis it may increase to 110 degrees It is the left main bronchus which tends to be pushed upward as the tissues are softer in children compression of the left main bronchus in mitral stenosis can occur and may cause pulmonary atelectasis

Pulmonary Edema The mechanism of this lesion has been explained in the first chapter It is often missing for reasons explained above

Prognosis

The prognosis in patients with rheumatic mitral stenosis in general depends upon many factors not the least of which is the frequency of recurrences of rheumatic fever and the condition of the myocardium When mitral stenosis is observed early in the course of rheumatic fever or after the active phase is over it may seem very slight and therefore the outlook may appear good But gradually and apparently without new attacks of rheumatic fever which can be diagnosed clinically a button hole mitral stenosis may develop and the patient succumbs within a few years At other times the lesion remains minimal and stationary these patients lead almost normal lives and reach old age Some live out their lives without being aware that heart disease exists

Despite such exceptions the average age at death from mitral stenosis is near forty years Most of these patients ultimately seek hospitalization for congestive failure

Surgical Therapy of Mitral Stenosis

The statements encountered in current literature in particular literature of surgical origin that mitral stenosis is essentially a surgical disease is a great simplification of the issue although it may be conceded that in certain stages medicinal therapy has little to offer This is true not only in advanced cases but in some patients even early when the heart is scarcely enlarged and the right ventricle functions perfectly but the pulmonary congestion is tremendous because of the mechanical obstacle of the stenotic mitral valve Here digitalis is of little help while surgery miraculously relieves the attacks of pulmonary edema dyspnea and hemoptysis

The idea of surgical relief is not a new one Sir Lauder Brunton suggested it long ago and Suttar performed the finger fracture procedure as early as 1925 The following year Pribram performed the operation from the ventricle Since procedures advised at that time resulted in a detrimental mitral insufficiency a high mortality and rare improvement operations were soon discontinued

Different Surgical Procedures Other surgical procedures were recommended all designed to diminish pulmonary congestion Bland and Sweet recommended an anastomosis between the right inferior pulmonary vein and the vena azygos Cossio and Perianes recommended tricuspid valvulotomy from the jugular vein

to create a regurgitation and relieve pressure in the lesser circuit and Cossio also ligated the inferior vena cava to reduce the right heart output others performed a sympathectomy to slow the heart All these efforts were soon overshadowed by two operations which proved safer since they did not usually create an appreciable insufficiency of the mitral valve mitral commissurotomy and the finger fracture method In both procedures one opens and enters the left atrium The finger fracture method is preferred if it is impossible commissurotomy is done With both methods the individual leaflets are separated no valvular tissue is removed but the orifice is enlarged

Indications and Contraindications Patients with mitral stenosis are divided into four groups or stages In stage I the lesion is asymptomatic In stage II the patient has symptoms at rest or effort but the complaints are static and do not progress In stage III the symptoms progress in spite of correct therapy In stage IV the complaints are incapacitating No operations are performed in stage I and they are seldom of use in stage IV they are indicated and useful in stages II and III These stages of course represent a rough distinction only A patient may show progressive complaints and failure (stage III) but the stenosis of the mitral valve is slight and not advancing however the myocardium is damaged by rheumatic fever and fails We recommend the operation in stage II only if pulmonary edema or hemorrhage is present or if the complaints are marked Stage III i e in progressive disease offers the chief indication but one must be sure — if possible — that progression of complaints is not caused by reactivation of rheumatic fever acute infection overexertion and so forth

The operation is not performed too early in childhood since mitral stenosis tends to be progessive and new deposits of fibrin repeatedly develop on the valves due to recurrences of rheumatic fever Successful postoperative cases are known in which the benefit of operation disappeared after a few years because the stenosis recurred Therefore although active rheumatic fever is a contraindication it is clear that this rule is too dogmatic In the first place signs of rheumatic activity have been found in 30 to 40 per cent of postoperative patients in the resected left atrial appendices In most instances no clinical evidence of activity existed Moreover if a patient with mitral stenosis congestive heart failure and active rheumatic fever is operated on the diminution of only *one* of these factors may be life saving

Subacute bacterial endocarditis is also a contraindication Operation is contraindicated in patients with marked irreversible cardiac dilatation One does not operate on patients having an appreciable aortic stenosis and regurgitation or a definite mitral insufficiency Studies with the gloved finger during operation have shown that mitral insufficiency causes a regurgitating jet and that its presence of a slight degree does not contraindicate the operative procedure while a definite mitral regurgitation does The difficulty of diagnosing a mitral insufficiency will be discussed in the following section

We advise the operation in patients with increasing disability According to Wood surgery is required in 50 per cent of all patients with mitral stenosis

Since after the age of twenty years recurrences of rheumatic fever are less common some physicians prefer to operate on patients under 20 In patients over 40 years old complications occur more often and the mortality increases

The patient should be digitalized before the operation neither atrial fibrillation nor a history of pulmonary embolism is a contraindication However the operation cannot always be carried out since occasionally the atrium is filled with thrombi Surgery is not advised if there is no evidence of an increased resting pressure in the pulmonary arterial system or when one suspects that pulmonary pressure is increased because of left ventricular failure (Cournand et al)

Results of Operation The operative mortality varies according to the surgeon and to the stage in which the patient is operated on Thus in one series no patient died in stage II while 4 6 per cent died when the operation was performed in stage III the immediate operative mortality in stage IV was 31 per cent The average mortality is reported as between 6 6 and 27 4 per cent Embolism in the systemic circulation occurred in 6 per cent of the operations Harken reports a mortality of only 1 per cent in patients in stage III while it was 27 per cent in stage IV

A serious complication is a systemic embolism from dislodged thrombi in the left atrium At the present time owing to Bailey s method of compressing the carotid arteries and permitting the blood to gush out and carry the thrombotic material with it the incidence is somewhat diminished But many surgeons abandoned this procedure A rare but serious complication is dissection of the left circumflex coronary artery or subacute bacterial endocarditis caused by staphylococci (Dalton et al)

While the operation brings dramatic relief in some cases it lacks success in others Prediction is impossible at present The operation is rarely curative however In 214 patients one group of surgeons saw 41 6 per cent greatly improved 7 per cent improved and 13 0 per cent unimproved Bland reports an improvement varying between 58 3 and 86 0 per cent The salvage rate of surgery in class IV patients according to Denton and Bolton is as follows there was an immediate mortality of 12 of 61 patients nine died within one month Of 38 living patients 33 showed distinct improvement

No proof has been given that mitral surgery diminishes the incidence of systemic embolism Despite marked clinical improvement the change of heart size and shape and of the electrocardiogram are often insignificant An improvement may appear 4 to 6 months following surgery Disappearance of the increased pulmonary resistance seems to require time

Clover examined 50 patients five years after the operation In 20 the results were excellent 16 were improved and 5 unimproved The others had died Baker et al found the results in 18 out of 45 postoperative patients not favorable three years after the operation

The final results — the frequency of re stenosis the ultimate effect of surgery as to duration of life — cannot as yet be evaluated

The diastolic murmurs may become shorter or may disappear Even if they remain unchanged improvement may be great The size of the heart may diminish or increase the latter because of the better filling of the left ventricle The first heart sound over the apex and the second pulmonic sound may be less accentuated after successful surgery

Ideal Subject The ideal subject for surgery has a snappy apex beat and a very loud apical first sound (which disappears in an appreciable mitral regurgitation) There is a clearly audible opening snap (which disappears in marked regurgitation in rigid calcified valves which respond poorly to surgery and finally in marked pulmonary hypertension) In mitral regurgitation an audible third heart sound replaces the opening snap (Wood) The aortic knob is absent and the left ventricle not large There is typical widening and slurring of the P waves in leads I and II

Postcommissurotomy Syndrome An interesting complication of the operation is the postcommissurotomy syndrome which appears a few weeks after surgery The incidence of this syndrome has been found to be around 24 per cent It is known that rheumatic fever may be reactivated after trauma In the syndrome the patient develops joint and chest pain fever leukocytosis pericarditis and pleurisy While some authors believe that pulmonary emboli and the pericarditis which follows every entry into the pericardium even under sterile conditions are responsible we think that the appearance of a prolonged P—R interval in the electrocardiogram of some of these patients and the occasional marked increase of the antistreptolysin titer favor the assumption of a recurrence or reactivation of rheumatic fever Dressler calls attention to the striking resemblance between idiopathic pericarditis and the postcommissurotomy syndrome Different mechanisms may be responsible in different cases

Pathophysiology The contributions of surgery to better understanding of the pathophysiology of this lesion are considerable

Astonishing was the finding that in most patients examined by surgeons the size of the mitral orifice was 1 square cm or less The cardiac output may fall to 2 liters per minute or less (Dexter et al) Even in patients who were asymptomatic (stage I) the orifice was found so small that the fingertip could not pass through it even orifices of 0 3 square cm have been seen Surgery is very successful even if it increases the diameter only to 1 5 square centimeters This is remarkable because one would have assumed that some patients with a damaged myocardium develop cardiac failure in earlier stages In any event in agreement with experimental findings and in analogy with the aortic orifice reduction of the mitral orifice to one fourth normal which is about 1 square cm seems to be the critical value Under these conditions the pressure head necessary for adequate filling of the left ventricle must be considerable

The mechanism of pulmonary hypertension in mitral stenosis has always puzzled clinicians An increased pressure in the pulmonary veins is easily understood Why should this lead to an increase in pressure in the pulmonary arteries? Anatomic changes have been found in the pulmonary arterioles these however

are of a secondary nature the consequence and not the cause of hypertension in the lesser circuit Catheterization revealed that pulmonary vascular resistance rises early in many cases to a multiple of the normal values The mechanism is unknown and reflexes from the dilated pulmonary veins have been postulated We shall see in the chapter on cor pulmonale that local hypoxia in the lung makes pulmonary arterioles contract by a direct action on their smooth musculature Teleologically regarded this narrowing of arterioles may be considered beneficial since it prevents the appearance of excessively high pressures in the pulmonary capillaries and may explain why pulmonary edema is so rare in patients with advanced mitral stenosis It is certainly much rarer than recent reports maintain On the other hand even with mitral orifices of 0 5 square cm normal pulmonary resistance was found so that the mechanism of its development is not clear

Procedure It is the duty of the physician whenever he advises a patient regarding mitral surgery to consider prognosis without surgery the mortality of surgery and the complications of the procedure It is not ethical to tell the patient that he will be cured It is purely fortuitous if the mitral valve regains normal function after finger fracture or commissurotomy Usually the orifice becomes wider by only a few millimeters yet it is astonishing how much improvement such enlargement may bring

MITRAL REGURGITATION

Etiology

Rheumatic Fever Verrucous endocarditis renders the mitral valve incompetent by retracting the thickened leaflets and by shortening the chordae tendineae Rheumatic mitral insufficiency is usually combined with stenosis owing to fusion of the valves Pure mitral regurgitation of rheumatic origin without any evidence of a stenosis is rare Often the stenosis is silent and no diastolic murmur is audible In performing a commissurotomy with the finger in the left atrium Bailey missed the typical regurgitation jet in one third of 1 000 patients Mitral regurgitation is a little more common in men than in women

Relative Mitral Insufficiency Valvular incompetence without organic changes in the leaflets is a very common event in all conditions associated with marked dilatation of the left ventricle It is a typical complication of hypertension aortic insufficiency and myocardial lesions Two forms can be distinguished In one the valvular ring may widen because of a pronounced left ventricular dilatation so that the valves are unable to close in systole In the other and more common variety the heart dilates along the axis of the ventricle this displaces the papillary muscles downward and the chordae tendineae prevent the valves from closing completely

Malformations and Trauma Mitral insufficiency due to malformations or caused by trauma are rare In a traumatic case personally observed by one of us a bullet created a small hole in one leaflet of the mitral valve (Adam)

Atherosclerosis Not rarely atherosclerosis increases the thickness of the aortic leaflet of the mitral valve but this rarely makes the valve incompetent Simon and Liu found calcification of the annulus of the mitral valves in 10 per cent of 590 unselected consecutive necropsies

Dynamics

In mitral insufficiency blood returns to the left atrium under high pressure during ventricular systole In experimental mitral insufficiency more than 50 per cent of the stroke volume may regurgitate

In order to overcome the diastolic intra aortic pressure and to eject its contents into the aorta pressure within the left ventricle must exceed aortic diastolic pressure Due to the loss of blood by leakage through the mitral valve this level of intra aortic pressure is reached later than under normal conditions Since pressure in the left atrium is much lower than that in the aorta it is not clear why the left ventricle does not send its entire output into the atrium According to Wiggers the great vigor of contraction causes intraventricular pressure to rise so rapidly that the resistance of the diastolic intra aortic pressure is overcome The more the myocardium is damaged the weaker the systole and the greater the loss of blood into the left atrium

Symptoms

The complaints are similar to those of mitral stenosis Exertional dyspnea appears early and is the outstanding symptom during the entire course of the disease There are no symptoms specific for mitral insufficiency

Signs

Palpation As in mitral stenosis palpation shows evidence of hypertrophy of the right ventricle as revealed by diffuse pulsations over the precordium The second pulmonic sound may be palpable Early however the apex beat is displaced downward and outward since the left ventricle is dilated from the beginning If the apical murmur is low pitched a systolic apical thrill is sometimes palpable In some patients the unusually large left atrium reaches far into the right chest and systolic pulsations are found to the right of the sternum between the fourth and sixth ribs These pulsations are rather strong owing to the systolic distention of the left atrium by ventricular pressure The proximity of left atrium to the anterior chest wall is favored by the rotation of the heart around its axis to the left

The heart is mitralized with evidence of marked enlargement of the left atrium and left ventricle

Auscultation the Systolic Murmur Auscultation reveals an apical systolic murmur Since murmurs of this kind are often heard in the healthy it is proper to discuss first the systolic apical murmurs encountered in healthy individuals that are so often confused with those of a real mitral insufficiency

The nomenclature is difficult One usually separates the organic murmurs of mitral insufficiency from the functional or 'accidental murmurs of healthy people The term functional is not precisely appropriate for murmurs caused by organic changes also depend upon functional alterations Therefore it has been proposed to differentiate between physiologic and pathologic murmurs Naturally a pathologic systolic apical murmur will not always be due to a mitral insufficiency as there are many other causes for it It has also been proposed to differentiate between significant and nonsignificant or incidental murmurs

Physiologic murmurs are common In fact many physicians who have reflected on the matter have wondered why a systolic murmur is not heard over every heart under normal conditions When it is recalled how forcibly blood is ejected through narrow ostia into tortuous vessels the usual absence of systolic murmurs is indeed astonishing

Systolic murmurs are quite common in healthy young people Among 218 apparently healthy individuals in the first four decades of life Thayer found a systolic murmur in almost one third Examination of 5541 high school students revealed a nonorganic systolic murmur in 86 63 per cent (Schwartzman) Parkinson and Hartly found systolic murmurs in 10 per cent of healthy recruits Among those not presenting a murmur at rest over 80 per cent develop such a murmur after exercise These murmurs are heard most often over the pulmonary artery and they may disappear in the erect position Sometimes they are very loud and rough but only rarely are they accompanied by a thrill

These physiologic murmurs are less frequent in adults They do however occur at all ages Since a murmur irrespective of its origin depends as pointed out earlier on a certain velocity of the blood flow these murmurs often become *louder or appear on exertion Other physiologic murmurs are audible only at rest* They may be blowing rasping mewing or musical If by chance an opportunity is afforded for the examination of such a heart at necropsy no alteration capable of evoking the murmur may be discovered

Acceleration of the blood flow in anemia or for other reasons may cause a systolic murmur These murmurs appear over all ostia in anemia (Laennec s murmur) and are constantly heard over the base of the heart Formerly they *were accounted for by a diminished viscosity of the blood but undoubtedly the* increased velocity of blood flow is the real causative factor In anemic patients highly musical systolic murmurs may be audible over the large veins near the base of the heart (venous hum) In rare cases the latter are heard even during diastole Loud systolic murmurs (hemic murmurs) and cardiac enlargement in anemic patients may simulate primary cardiac disease

Systolic murmurs appear regularly in fever as the result of increased velocity of blood flow If the fever is of unknown origin a loud systolic murmur over the heart may focus the attention on this organ (a subacute bacterial endocarditis is often suspected) and this may lead to lack of recognition of the real cause for the fever Hyperthyroidism is almost invariably associated with systolic murmurs owing to the acceleration of the circulation

Differentiation between physiologic and organic murmurs is extremely important In patients who have had rheumatic fever in the routine examination of school children in physical examinations for employment for military recruits or for insurance companies the question constantly arises how to interpret a systolic murmur at the base or apex

It is important to remember that every systolic murmur should arouse suspicion This is especially true in the older patient and if it was absent previously Therefore every effort must be made to rule out a pathologic process

Since the differentiation between physiologic and pathologic murmurs concerns a problem that confronts the physician almost daily several methods for arriving at a decision have been recommended

(1) Considerable emphasis has been placed in the past on the fact that murmurs of mitral insufficiency are transmitted to the back while physiologic murmurs are heard only over the heart This rule has little value The transmission of a murmur to the back depends merely on its loudness and its pitch and not whether it originates in an organic lesion of the valve

(2) Levine as pointed out before differentiates six degrees of a systolic murmur It is often stated that murmurs beyond grade 2 are pathologic This is not in accord with our experience It is true that louder murmurs are more suspicious however they are not invariably pathologic Cardiac surgery has also revealed that even in the presence of a grade 3 apical systolic murmur no regurgitating jet could be detected at operation

(3) The absence of the first sound at the apex (occasioned by the mitral incompetency and change in the presphygmic period) has value for the diagnosis of mitral insufficiency if a systolic murmur is audible at the apex Since mitral regurgitation is usually accompanied by mitral stenosis which accentuates the first apical sound this rule often is not reliable

(4) Whereas the physiologic systolic murmur may be very loud the murmur in a true case of mitral insufficiency may be soft and faint The intensity of the murmur does not permit any conclusion concerning the extent of the valvular lesion A slight valvular incompetence is associated with regurgitation of blood through a narrow opening into the left atrium and the murmur may be loud In a more advanced mitral insufficiency the communication between the left ventricle and atrium is broad and sometimes no murmur at all or merely a very faint murmur is audible

One may say that if two patients present exactly the same murmurs over the mitral valve it is entirely possible that one has an organic mitral regurgitation and the other a healthy heart with a physiologic murmur

(5) Considerable stress is often placed upon the accentuation of the second pulmonic sound in mitral lesions This sign is unreliable since it is absent in early stages of mitral regurgitation as long as pressure is not increased in the lesser circuit and is likewise absent in the later stages when right ventricular failure appears with a consequent fall of pressure in the lesser circuit Moreover a loud second pulmonic sound is physiologic in healthy young people Therefore

if such individuals present a loud apical systolic murmur and in addition complain of palpitation and dyspnea an erroneous diagnosis of mitral regurgitation is sometimes made Since the diagnosis of a valvular lesion has a profound effect on the patient and may influence his whole life in many ways this diagnosis should not be made casually Too often one sees patients with healthy hearts in whom the diagnosis of an organic heart disease was made many years ago simply on the basis of a systolic apical murmur



FIG 34 Rheumatic mitral lesion with regurgitation predominating enlarged left ventricle

(6) Frequently it is said that a distinction between physiologic murmurs and those due to mitral insufficiency is possible if the patient is examined in different postures The murmur of mitral insufficiency is loudest if the patient is recumbent while physiologic murmurs are intensified in the erect posture It is true that the murmur of mitral insufficiency as well as those of mitral stenosis often are detected only in recumbent patients Functional murmurs however sometimes have the same peculiarity and therefore no decisive conclusion can be drawn from this fact alone

As a corollary to the preceding discussion it follows that the diagnosis of a mitral insufficiency should never be made from auscultatory findings alone Only those who follow this rule will avoid errors of serious consequence *In the presence of a systolic apical murmur mitral regurgitation should be diagnosed only if the left atrium and ventricle are enlarged*

Left Atrium and Ventricle Whereas in mitral stenosis dilatation of the left atrium may be absent for a long time this dilatation occurs early in mitral regurgitation In mitral stenosis the left atrium may overcome the obstruction by means of hypertrophy alone at least for some time In this lesion the atrium dilates secondarily if compensation by simple hypertrophy is impossible On the other hand in mitral insufficiency the left atrium dilates from the beginning (primarily) because with valvular incompetence the left atrium fills from both sides backwards and under high pressure from the ventricle as well as normally from the pulmonary veins The dilatation of the left atrium may be enormous the term aneurysm has sometimes been applied to it

Parallel and coincidental to the atrial dilatation the left ventricle also dilates since in a pure insufficiency the patent mitral orifice permits the left ventricle to overfill in diastole (figure 34)

If enlargement of the left atrium and ventricle cannot be demonstrated by percussion *fluoroscopic examination becomes necessary to confirm the diagnosis* The finding of an esophageal displacement in the right anterior oblique position is often decisive for the diagnosis If no abnormality is revealed by this examina tion it is well to re examine the patient after a few months The diagnosis of a mitral insufficiency may be discarded if the left atrium remains normal A normal left atrium and left ventricle are found only in patients with negligible mitral insufficiency

Electrocardiography

This gives no assistance in the diagnosis of a mitral insufficiency With hypertrophy and dilatation of the right and left ventricle there is often no axis deviation

Catheterization and Diagnosis During Surgery

When during cardiac catheterization the tip of the catheter is wedged into a small pulmonary artery and the pressure registered it is claimed that a large systolic pulse wave appears in the presence of mitral regurgitation This sign however proved unreliable With a finger in the left atrium the surgeon can readily feel the regurgitating jet and — from its strength — can draw a conclusion as to the degree of regurgitation With this method mitral insufficiencies were discovered when no systolic murmur existed at the apex on the other hand as pointed out before loud systolic murmurs have been found with no evidence of mitral regurgitation a lesion of a different degree than the clinician had concluded from the loudness of the murmur may be found

Other Diagnostic Methods In pure or predominating mitral insufficiency there is no opening snap and no accentuation of the first apical sound Gallop rhythm occurs Systolic expansion of the left atrium can be seen fluoroscopically but often is missed these expansions have been registered in the esophagogram fluorocardiogram and kymogram All these methods of examination contribute very little If in a proven mitral stenosis roentgen examination particularly

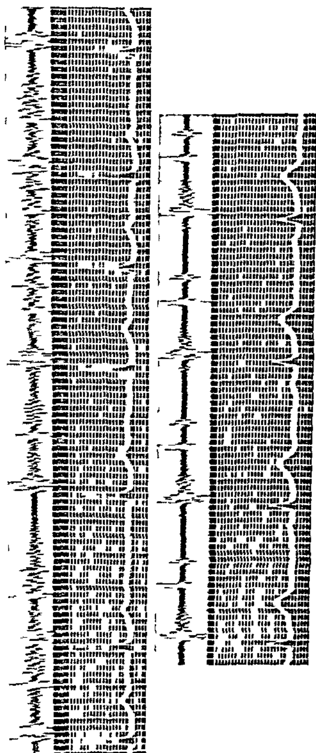


Fig 35 (a) Obtained at the apical area from a 54 year old woman with mitral regurgitation and stenosis and atrial fibrillation a blowing systolic and a rumbling diastolic murmur were heard (b) Obtained from a 22 year old woman with rheumatic mitral regurgitation the tracing was obtained at the cardiac apex and shows a systolic murmur and gallop rhythm

in the left oblique position reveals an enlargement of the left ventricle there is a strong probability in favor of a mitral insufficiency but an aortic lesion must also be ruled out In the latter the aortic knob is well developed while it is usually missing in pure mitral lesions

Differential Diagnosis

The outstanding problem in differential diagnosis of a mitral insufficiency is the distinction of the systolic apical murmur from a physiologic murmur (This was discussed in the preceding pages) The differentiation between an organic and a relative mitral insufficiency (which was often called functional) is easy if there is a diastolic murmur indicative of mitral stenosis (figure 35) This can only mean a rheumatic etiology If however the systolic apical murmur alone is found and the heart displays a mitral configuration relative as well as organic mitral insufficiency may be present Gallop rhythm (figure 35) occurs in both forms of mitral regurgitation If the signs of the valvular lesion disappear during treatment one may properly assume the existence of a relative mitral insufficiency which disappeared when the state of the heart muscle improved Otherwise only careful investigation and the demonstration of some disease which might lead to marked dilatation of the left ventricle and a relative insufficiency of the valve permit one to reach a differential diagnosis Occasionally the history will assist A patient with a rheumatic lesion of the mitral valve complains of increasing exertional dyspnea A patient with relative mitral insufficiency presents typical paroxysmal nocturnal dyspnea characteristic of left ventricular failure

It should be kept in mind that relative mitral insufficiency is a complication of some heart lesion and is *not an entity sui generis*

Prognosis

Statements concerning the outlook for a patient with mitral insufficiency should be guarded In older reports the prospect was often described as excellent This is understandable because rather often the diagnosis was made in healthy individuals with a physiologic murmur If the diagnosis however is limited to real cases of mitral insufficiency it is soon discovered that patients with mitral insufficiency or a double mitral lesion with a predominating insufficiency develop the picture of complete and irreversible decompensation in a relatively short time This is partly due to the early and sometimes enormous dilatation of the left atrium and ventricle

The combination of mitral insufficiency with stenosis has its favorable aspects the stenosis prevents overfilling and dilatation of the left ventricle even when the left atrium is markedly distended

Surgical Therapy This is still in the experimental stage and it is too early for a proper evaluation Venous and pericardial grafts have been used in dogs Mitral suturing has been attempted With deformities of the valves mitral commissurotomy may decrease the degree of regurgitation but often results in an increase

TRICUSPID REGURGITATION

This lesion is still frequently overlooked by physicians who rely largely on auscultation for the diagnosis of valvular lesions The diagnosis however, is often readily made by other methods

Etiology

Isolated rheumatic involvement of the tricuspid valves is extremely rare A combination of rheumatic valvulitis of the mitral aortic valves and evidence of a similar process in the tricuspid valves is common Various statistics indicate that careful examination will disclose tricuspid valve involvement in 20 to 30 per cent of the patients with rheumatic mitral disease

There are rare instances of an isolated tricuspid insufficiency resulting from healed bacterial endocarditis

A relative tricuspid insufficiency due to dilatation of the right ventricle is the type most often encountered It may be present with a moderate dilatation of the right ventricle or absent when there is considerable dilatation It is commonly associated with rheumatic mitral lesions which lead to an enlargement of the right ventricle and with myocardial diseases of various etiologies One case of a relative tricuspid and mitral insufficiency developing in the course of intractable paroxysmal ventricular tachycardia which lasted for years has been described elsewhere (Scherf and Kisch)

Congenital tricuspid insufficiency due to malformation of the valve is also known (Barritt and Urich)

Dynamics

If the tricuspid valves are incapable of closure a certain amount of blood is sent back into the right atrium during systole Right atrial dilatation develops early and is accompanied from the beginning by dilatation of the right ventricle In an uncomplicated case the regurgitating blood fills the right atrium without creating any abnormal sign If congestion increases however or if the atria fibrillate regurgitation even of small quantities of blood provokes certain easily detected signs

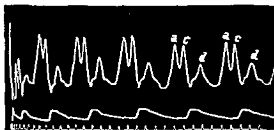
In an advanced tricuspid insufficiency the left ventricle is said to undergo atrophy due to inadequate filling

Symptoms

It is characteristic for patients with tricuspid regurgitation to have but few complaints There is no dyspnea unless physical exertion exceeds certain modest limits No orthopnea or paroxysmal nocturnal dyspnea are observed Sleep is undisturbed Digitalis in remarkably small amounts and above all diuretics keep these patients well for a long time

Signs

Positive Venous Pulse The diagnosis is often possible by inspection In healthy people a venous pulsation composed of three waves can often be observed in the neck veins Figure 36 a shows a normal venous pulse The first wave (the a wave) arises during and in connection with atrial systole while the c wave and v wave arise *during ventricular systole During a large part of ventricular* systole blood is expelled into the peripheral arteries thus increasing the negative pressure within the chest this facilitates the inflow of blood into the chest so



a



b

FIG 36 (a) Normal venous pulse (b) A positive venous pulse in a patient with tricuspid regurgitation and atrial fibrillation the fibrillation waves are visible in the venous pulse

that the neck veins are not engorged Accordingly there is a deep collapse between the c and v (or d) waves The normal physiologic venous pulse is called negative because of this depression during a good part of systole

With marked congestion and particularly when atrial fibrillation co exists the systolic collapse in the venous pulse may become less distinct or may disappear entirely without a tricuspid insufficiency being present The reason for this is as follows ventricular systole has little or no effect on the venous blood flow in advanced stages of congestion the veins remain constantly distended and may show no pulsations at all This can be demonstrated even in beginning right heart failure by pressure on the right upper abdomen Such pressure increases the return of blood to the right heart and distends the veins to a greater extent and for a longer time than under normal conditions and abolishes pulsations of the vein

In tricuspid insufficiency the systolic regurgitation of blood into the right atrium may cause the transmission of a pulsation into the neck veins, a finding that becomes increasingly obvious if the atrium and the veins are overfilled due to congestion The collapse between the c and v waves disappears both waves merge into a single large one and the venous pulse is ' positive Figure 36b shows a positive venous pulse from a patient with tricuspid insufficiency Atrial fibrillation is also present in this patient and therefore the a waves are abolished

In tricuspid insufficiency the back flow of blood under the high pressure created by ventricular systole causes a visible pulsation in the neck If the jugular veins are compressed halfway along their course this pulsation is still visible below the point of compression This shows that a real backflow from the heart is responsible

The pulsations are often absent from the superficial neck veins for these vessels are so distended that they cannot pulsate The vein in which the pulsations are distinct is the deep jugular vein which is covered by the sternocleidomastoid muscle As the result of persistent regurgitation of blood under ventricular pressure the vein wall distends Often the internal jugular vein is so wide that at necropsy three fingers can easily be introduced into the lumen without stretching it In such cases a broad pulse wave ascends the neck with each systole and lifts the sternocleidomastoid muscle It ascends up to the lobe of the ear Students often confuse these strong pulsations with the Corrigan pulse of aortic insufficiency For differentiation one can easily discover that peripheral arteries do not show a collapsible pulse while palpation of the pulsating vessels reveals the low venous pressure Furthermore the pulsation is not jerky but ascends relatively slowly

The pulsations are usually most distinct on the right side for the right innominate vein ascends in direct continuity whereas the left departs from the superior vena cava at approximately a right angle In rare cases we have seen a stronger pulsation on the left presumably the result of an anatomic anomaly in these vessels

With marked venous stasis the pulsations may be visible only when the patient is erect *in this position the pressure within the neck veins diminishes some*what as the inflow of blood into the right atrium improves This leads to less distention of the vessel and permits pulsations to appear Often venous pulsations are absent in all positions but reappear as soon as successful treatment lowers the venous pressure In early cases the huge right atrium can accept regurgitating blood and no abnormal venous pulse is noted in the neck In these cases the characteristic pulsations appear only in the recumbent position or if the amount of blood flowing back to the right heart is increased by compression of the right upper abdomen

Some patients are profoundly distressed by the regurgitation of blood into the neck veins at least when this first happens They suffer from throbbing in the ears probably owing to the impact of the regurgitating blood on the bones enclosing the veins in the head the pulsations are regular with sinus rhythm

and irregular in fibrillation The patient can readily count the heart rate by the throbbing alone This sensation is aggravated by certain positions of the head and is diminished in others A general oppression is felt in the neck as the result of increased systolic filling of all deep veins

Positive Liver Pulse The blood driven back into the right atrium by ventricular systole does more than reach the tributaries of the superior vena cava It also flows back into the domain of the inferior vena cava particularly through the wide open valveless hepatic veins A systolic swelling of the liver a systolic liver pulsation is the result

Systolic pulsations of the liver occasionally occur without tricuspid insufficiency Massive right ventricular hypertrophy may thrust the liver downward when the impact of cardiac systole is transmitted through the diaphragm The abdominal aorta may push the liver ventrad in the midline Like other organs the liver may show systolic pulsations if there is an aortic regurgitation and the hepatic arteries pulsate strongly Local systolic pulsations may occur in the neighborhood of a liver abscess

The hepatic pulsation of tricuspid insufficiency can be differentiated from the above mentioned forms for it is expansile The liver volume increases in all directions a fact easily discovered if both hands are applied at some distance from each other By this means the systolic increase of the liver volume is readily distinguished from a transmitted cardiac or aortic pulsation In early cases the pulsation is absent since the pressure of regurgitating blood is not sufficiently high to distend the liver We have seen it disappear during the course of the disease when the amount of fibrotic tissue in the liver increased and cirrhosis developed The enlarged liver is not tender unless congestion develops acutely or is of recent origin

At times systolic pulsations may be noted in other regions such as the spleen or the peripheral veins Pulsations of the veins of the forearm and of other peripheral vessels occur but with less regularity and less characteristically than the positive venous and hepatic pulse The venous pulsations in the arms may be demonstrated by raising the arm almost to the level at which the veins collapse

Pulsations of the Chest Marked liver pulsation causes a distinctly perceptible movement of the right upper abdomen to the right The hypertrophy and dilatation of the right ventricle simultaneously displace the thorax to the left so that a characteristic see saw movement is visible

Inspection reveals the systolic retraction of the interspaces over the precordium which is typical for right ventricular hypertrophy and dilatation and there is a strong diastolic bulging

Ascites Edema The great stasis created in the portal circulation by the systolic regurgitation of blood into the liver produces ascites another sign characteristic of a fully developed tricuspid insufficiency It is rarely absent In many cases ascites is the outstanding feature and requires the continuous administration of mercurial diuretics At present in many cases paracentesis

can be avoided or postponed for years by the skillful employment of these compounds In the course of time more or less evidence of cardiac cirrhosis may appear

Edema is common in relative tricuspid insufficiency and anasarca is not rare The edema may vanish while the ascites persists The appearance of edema may coincide with effusions into the serous cavities

Cyanosis Despite enormous dilatation of the right heart cyanosis is often absent It has been pointed out earlier that with the appearance of right ventricular failure and the development of hepatic congestion cyanosis if previously present may vanish If right heart failure develops acutely the patient may even show marked pallor owing to the retention of quantities of blood in the liver and veins In accordance with these events x ray examination discloses relatively clear lung fields in tricuspid insufficiency



FIG 37 Typical orthodiagram from a patient with tricuspid regurgitation

Percussion and X ray Examination This provides evidence of dilatation of the right atrium and ventricle These findings are not characteristic because they appear regularly in certain stages of the underlying accompanying condition (rheumatic mitral lesion or myocardial disease)

The dilatation of the right atrium however may reach considerable dimensions (figure 37) The vascular band widens owing to the congestion of veins near the heart

Auscultation The systolic murmur one might expect to hear at the lower end of the sternum at the site of auscultation of the tricuspid valve is absent in most cases While the mute variety is exceptional in other valvular lesions it is the rule in tricuspid insufficiency Contrary to statements by many authors in a large series of patients with tricuspid insufficiency with the diagnosis confirmed at necropsy we gained the impression that a distinct murmur over the tricuspid area is an exceptional finding To be sure systolic murmurs are often detected in this area however one cannot be certain that they are not transmitted from the mitral or pulmonic valve Although a murmur heard over the tricuspid area may sound different at this point from one at the mitral area this does not mean there are two different murmurs The characteristics of a murmur may be changed more or less through transmission because the tissues filter it

The reason for the frequent absence of a separate systolic murmur over the tricuspid area in tricuspid insufficiency is not known The valve is not situated deeply and conditions for transmission to the surface of the thorax are good In many cases it seems that the murmur is conducted better to the apex and is

then confused with a mitral murmur This mistake is more apt to occur in those cases where the heart rotates to the left when the right ventricle dilates

The statements in the preceding paragraphs disagree with those of many authors (Muller and Shillingford) who found a murmur in the fourth intercostal space to the left of the sternum to be the earliest and best sign of tricuspid incompetence

The second pulmonic sound is rarely accentuated The signs of aortic incompetency may disappear when a tricuspid regurgitation develops

Differential Diagnosis

Differentiation between a relative and an organic tricuspid insufficiency is not possible as a rule on the basis of the clinical findings Even if evidence of tricuspid regurgitation appears during decompensation it is possible that regurgitation was present before but evoked no signs to permit the diagnosis In a similar way the disappearance of signs of tricuspid regurgitation during successful treatment may be due simply to diminished congestion and does not necessarily signify that a relative tricuspid insufficiency has disappeared It has been claimed that in tricuspid lesions caused by valvular disease the systolic venous wave appears later and reaches its peak later than in relative tricuspid insufficiency Only in a pure myocardial lesion may one assume that the signs of tricuspid insufficiency appearing during decompensation are due to a relative insufficiency

Cardiac catheterization reveals a higher diastolic atrial pressure compared to that in the right ventricle (Whitaker)

Prognosis

The frequently expressed opinion that the appearance of a tricuspid regurgitation signifies a serious complication of bad prognostic significance cannot be accepted without reservation Patients with an organic (more rarely with a relative) tricuspid insufficiency have been under our observation for more than eight years and have remained in a tolerable condition The greatest danger to which these patients are exposed is pulmonary embolism

The safety valve function of a tricuspid regurgitation in relieving the pressure in the lesser circuit was described as early as 1837 by King

TRICUSPID STENOSIS

Etiology

This lesion is an occasional sequela of a rheumatic involvement of the tricuspid valves and under these circumstances always accompanies a rheumatic mitral and/or aortic lesion It is much more common in women than in men In rare cases congenital tricuspid stenosis is produced by a malformation in this variety *other malformations particularly atrial septal defects* are usually present *The tricuspid stenosis in metastasizing carcinoids* will be discussed later

Symptoms and Signs

There are no characteristic symptoms or signs The diagnosis is made only on the basis of a syndrome that is not entirely typical and that hardly amounts to more than a suspicion

Patients with tricuspid stenosis are usually cyanotic and have a definite yellow complexion (subicterus) The right atrium is very large The neck veins are congested and show presystolic pulsation (an accentuated a wave) The presystolic venous (and liver) pulse can be registered by graphic methods they are not pathognomonic for they may be noted in other conditions e g pericardial adhesions One may palpate a bifid liver pulsation Clubbing of the fingers is common and a polycythemia is often noted The peripheral pulses are small

On percussion and x ray examination the heart shows a pronounced dilatation to the right since the right atrium enlarges The vascular band at the base of the heart is wide owing to dilatation of the veins The lung fields are clear there is no pulmonary congestion

Auscultation usually reveals no abnormality Sinus rhythm is common In some exceptional cases rumbling diastolic murmurs are said to be audible at the lower left sternal border We have never found them despite the observation of a number of cases verified at necropsy

An opening snap is heard over the tricuspid area or to the right of it it appears about 0 1 second after the onset of the second sound (Kossmann)

The liver is markedly enlarged and ascites is frequently found All these signs depend upon the fact that the right atrium is unable to empty its contents normally into the right ventricle and therefore some blood returns to the veins during atrial contraction (in presystole) Sometimes the right ventricle is smaller than normal just as the left ventricle is atrophic in mitral stenosis Large P waves are seen in the electrocardiogram

Catheterization may reveal a higher mean pressure in the right atrium The resting cardiac output is reduced (Ferrer et al)

Diagnosis

If there is pronounced dilatation of the right atrium and massive congestion of the liver in a patient with rheumatic mitral or aortic valvular disease without evidence of tricuspid insufficiency or pericardial adhesions and if the patient shows cyanosis and some jaundice the presumptive diagnosis of tricuspid stenosis is justified If there is no fibrillation the presence of presystolic pulsations of the jugular veins and of the liver gives some support to this diagnosis The diagnosis is also probable but unproven when an expansile liver and positive venous pulse gradually diminish in a tricuspid insufficiency despite increasing cardiac dilatation and decompensation In this case one may justifiably assume the existence of a tricuspid lesion in which an increasing stenosis progressively displaced the signs of insufficiency

Pulmonic Regurgitation

Etiology

Rheumatic involvement of the pulmonic valve is exceedingly rare Occasionally bacterial endocarditis causes pulmonary regurgitation and even more rarely the endocarditis heals leaving the patient with a pure valvular insufficiency We have had the opportunity to observe only one case of this type but they will doubtless be seen more often since the introduction of the modern antibiotic treatment of bacterial endocarditis Congenital pulmonary insufficiency is likewise rare in such cases the number of cusps of the pulmonic valve is usually increased or decreased

Relative insufficiency of the pulmonic valve is much more common It seems to affect both sexes equally and to occur at all ages although the vast majority of cases are discovered in adult life In a majority of these cases a rheumatic mitral stenosis coexists If pressure is high in the lesser circuit as indicated by an accentuation of the second pulmonic sound and a wide pulmonary artery a soft diastolic murmur may appear in the second or third interspace to the left of the sternum (Graham Steell murmur) It has the same pitch and the same site as the murmur of aortic insufficiency It may be temporarily louder then vanish to reappear from time to time If insufficiency of the aortic valve has been diagnosed one is surprised to find these valves normal at necropsy

The murmur has been designated as the murmur of high pressure A considerable increase of pressure in the lesser circuit may produce such marked dilatation of the pulmonary artery and valvular ring that the valves — otherwise normal — are unable to close

If one has the opportunity to observe a large number of patients with mitral stenosis over a period of years relative pulmonary insufficiency is not rare Cabot observed it in 22 of 55 autopsied cases of mitral stenosis It disappears if pressure in the lesser circuit falls as the right heart fails or a relative tricuspid regurgitation develops it reappears if the former status is restored by treatment

The comparatively frequent occurrence of relative pulmonary insufficiency in mitral stenosis requires an explanation for it stands in striking contrast to the rarity of relative insufficiency of the aortic valve Undoubtedly one reason is found in the local anatomy The root of the pulmonary artery and the valvular ring is weaker than that of the aorta Another factor is the preference of rheumatic histologic changes to involve the conus of the pulmonary artery and the root of the artery itself Accordingly weakness or destruction of these structures makes the appearance of a relative pulmonic regurgitation easier if pressure rises in the lesser circuit

Relative insufficiency of the pulmonic valve also develops in other conditions which increase pressure in the lesser circuit e g in fibroid tuberculosis extensive myocardial lesions and kyphoscoliosis

There are no characteristic symptoms.

Signs

Invariably the second pulmonic sound is palpable and markedly accentuated in these cases unless emphysema coexists The conus of the pulmonary artery and the pulmonary artery itself are dilated Since the right heart enlarges markedly a very characteristic configuration pouter heart appears Figure 38 shows the orthodiagram obtained from a rheumatic mitral steno is and relative pulmonary incompetency showing the characteristic change of cardiac shape

According to Hall a diastolic thrill occurs only in the organic and never in the relative insufficiency of the pulmonic valve It has been found however in a case of relative pulmonic insufficiency that was examined at necropsy This should be expected because the intensity and pitch of the murmur rather than the etiology is decisive for the presence or absence of a thrill



FIG 38 Typical orthodiagram from a patient with rheumatic mitral stenosis and relative pulmonary insufficiency (pouter heart)

A loud systolic murmur over the pulmonary artery is heard in all cases It is explained by the dilatation of the pulmonary artery and the right ventricle (relative stenosis of the ostium)

On fluoroscopy a pulsus celer of the hilar vessels gives a very characteristic picture although it is not always present Hilar dance is not pathognomonic for it occurs in many condition as mentioned in the preceding chapters The lung fields are relatively clear since the relative pulmonary insufficiency acts like a safety valve for the lesser circuit and diminishes congestion Dilatation of the pulmonary artery occurring in mitral stenosis without relative pulmonic regurgitation is not typical

Differential Diagnosis

Relative pulmonic regurgitation is most often confused with rheumatic aortic insufficiency because the location and type of the murmur is the same for both lesions Therefore it should be strongly emphasized that auscultatory findings alone are not the basis for diagnosis All physical signs and the results of fluoroscopy must be evaluated The absence of peripheral signs of aortic insufficiency should not be used against the diagnosis of this lesion for a coexisting mitral stenosis may abolish the peripheral and even the auscultatory signs of aortic valve involvement

The correct diagnosis may also be difficult when there is a silent mitral stenosis Often a positive diagnosis must await necropsy

The prognosis depends upon the underlying lesion

Pulmonary Stenosis

Since pulmonary stenosis is ordinarily a congenital heart lesion and is often associated with other malformations discussion of its symptomatology will be deferred This seems particularly advisable since the symptoms signs and prognosis depend to a vast extent upon the associated conditions The pulmonary stenosis in carcinoids is discussed below

Combined Lesions of More than One Valve

The essential features of most combined valvular lesions have been mentioned in the preceding pages In a large majority the mitral lesions constitute the fundamental disturbance The prognosis depends not upon the number of valves involved but almost invariably upon the status of the myocardium

Mitral aortic and tricuspid lesions represent a common combination Under this circumstance the tricuspid lesion may be organic or relative These patients may remain in relatively good health for years despite the existence of a cor bovinum

Since diastolic murmurs may be absent in such combined lesions and non characteristic systolic murmurs alone may be present it may be difficult to decide whether a rheumatic trivalvular lesion exists or simply a decompensated heart from a myocardial disturbance or hypertension with relative mitral and tricuspid insufficiency

It must be stressed again that the systolic murmur of aortic stenosis may be louder at the apex than over the aortic area while the diastolic murmur of aortic regurgitation may be absent over the aortic area but may be very loud over the left lower sternal border

Sometimes only the presence of a pulsus celer of the aortic knob will indicate the presence of an aortic insufficiency in mitral lesions on fluoroscopy

For the diagnosis of a silent mitral stenosis in combined lesions no sign is of greater value than the accentuation of the first heart sound with the snappy apex beat

Often x ray examination and electrocardiography offer some assistance in the differential diagnosis of combined lesions The presence of widened and notched P waves in leads I and II will speak in favor of the presence of a rheumatic mitral stenosis The advantage or disadvantage of the different combinations of single valvular lesions has often been discussed Conclusions reached on this subject as a rule are merely speculative

Carcinoids and Valvular Lesions of the Right Side of the Heart

Recently a well defined and readily recognizable syndrome has been observed in connection with carcinoids of the small intestine with metastases (argentaffinoma) (Isler and Hedinger)

Among other interesting features the patients suddenly develop flushes and report rapid changes in the color of the skin (deep red or purple) particularly

induced by emotions or physical exertion sometimes permanently Cyanotic or white patches are temporarily visible Telangiectasias are common Watery diarrhea (up to 30 stools daily) and abdominal pains may occur along with right heart failure with edema and ascites, more rarely attacks of asthma appear

An intestinal carcinoid with metastases to the liver is regularly found The pulmonary and tricuspid valves become thick and stenotic or insufficient the valves of the left heart remain normal usually but may also be involved (McKusick) Marked thickening and swelling of the endothelium of the hepatic veins has been found (Hegglin and Zollger)

The secretion of a vasoactive hormone by the carcinoid tissue has been known for many years The carcinoid produces a substance called serotonin (Lembeck Thorson et al) which is under extensive investigation This compound 5 hydroxytryptamine which is vasoactive and may lead to an elevation of pulmonary blood pressure and bronchial constriction seems necessary for normal mental processes (Wolley) It is found in the blood platelets and can be easily recovered from clotted blood It is found physiologically in the intestinal mucosa produced by the argentophile cells and is therefore called enteramine (Erspamer) The platelets absorb it The substance seems to be inactivated to a great extent in the lungs so that the left heart is usually spared (Gobel et al) The valve lesions are not explained One is reminded of the valvular changes observed by Lillehei in arteriovenous fistulas A color test has been developed to detect the excretion of metabolites of serotonin (5 hydroxy indole acetic acid) in the urine (Hanson and Serin Sjoerdsma et al)

Thickening and fibrosis of the endocardium involves also the chordae tendineae and the wall of the ventricles it does not concern the valves exclusively

A high incidence of congenital cardiovascular anomalies has been reported in these cases (Spain)

Therapy is limited so far only to reducing the size of the tumor

Even after metastases occur the disease may last up to 20 years (Ritchie)

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Chapter 13

Diseases of the Myocardium

Introduction

THE TERM MYOCARDIAL DISEASE is applied to a heterogenous group of affections and includes by common consent primary lesions of the myocardium secondary involvement of the muscle in the course of various diseases as well as the myocardial damage associated with coronary artery disease The great significance of myocardial lesions in national health is obvious from their incidence

Students and young physicians who attend lectures and postgraduate courses often gain a false impression of the incidence and importance of myocardial disorders because valvular lesions with their richer symptomatology and abundance of demonstrable signs are presented much more often than the less colorful myocardial diseases In practice however the diseases about to be discussed are much more common

In these conditions more than anywhere else in cardiac patients a careful history and percussion are of paramount importance for the bedside diagnosis in many cases Without percussion a severely affected myocardium may seem normal to many physicians particularly when murmurs are absent Very often these patients present no signs that are easily detected by auscultation therefore physicians who rely on murmurs for the diagnosis of heart lesions without such laboratory aids as the x ray or the electrocardiogram will often overlook a serious cardiac affection Unfortunately a considerable number of doctors learn the clinical aspects of the diseases now to be discussed only after they have gained experience by serious mistakes

For a long time all myocardial diseases have been lumped together in one category Every cardiac lesion not caused by valvular involvement was regarded as the result of myocardial degeneration This was followed by an era of myocarditis when elaborate classifications of parenchymatous and interstitial myocarditis were developed For a time practically all myocardial lesions were discussed under this heading Monographs on myocarditis were written and oddly enough made no mention of myocardial inflammation (which alone obviously is myocarditis) Actually the lesions secondary to coronary sclerosis were exclusively described Ultimately there was a natural reaction to this unwarranted emphasis upon myocarditis and textbooks on cardiovascular diseases were written which did not even mention this lesion A more objective attitude is encountered at the present time

There are not many other subjects in cardiology which have undergone greater change in recent times With the advance in knowledge the clinical diagnosis has become po sible in many cases

MYOCARDITIS

Incidence

As in the earlier editions of this book we wish to stress at the outset that myocarditis is a common disease and that the attitude still prevailing in many quarters where myocarditis is regarded as uncommon is unjustified and incompatible with present knowledge Adequate data have accumulated to show that neither the incidence nor importance of this disease was correctly appraised in the past

Histologic examination of the heart in over 5000 necropsies on adults who died from other than a contagious di ease revealed myocarditis in 4 26 per cent The percentage was even higher in children i e 6 83 per cent (Saphir)

Pathology

Grossly the soft flabby yellow or brown muscle resembles the pallid heart seen in connection with marked cloudy swelling Microscopically nonsuppurative myocarditis shows granular and hyaline necrosis in small foci surrounded by interstitial collections of cells The infiltrate is composed chiefly of lymphocytes polymorphonuclear leukocytes and plasma cells at times large numbers of eosinophiles are encountered The amount of inflammatory edema varies and small hemorrhages may be observed

In some coccal infections (strepto staphylo pneumo and gonococcal) small multiple abscesses may form particularly in the left ventricle The histologic picture is that of a focal abscess surrounded by a dense cellular infiltrate Early death from the provocative sep is may preclude the detection of reparative processes

Common Varieties

Myocarditis may accompany local or general infectious diseases and it may be essential that is without apparent involvement of other organs Among the more important diseases in which myocarditis is known to occur the following must be mentioned

Rheumatic Fever It is universally agreed that myocarditis is extremely common in the acute phase of rheumatic fever some observers even consider it a constant phenomenon This conclusion is based largely upon histologic and electrocardiographic studies

The many cases of rheumatic myocardial damage the appearance of Aschoff bodies round cell infiltrations and changes in the coronary arteries leading to the occlusion of small vessels have been discussed earlier Occasionally symptoms or signs of rheumatic myocarditis lead to the diagnosis of active rheumatic fever

which earlier was unrecognized This lesion has been discussed in the chapter on rheumatic fever

Tonsillitis Not rarely tonsillitis as well as other infections of the throat provoked by hemolytic streptococci cause an acute myocarditis In some cases *evidence of cardiac participation is obtainable one or two days after the onset of* tonsillitis more frequently it appears 6 to 8 days after the throat infection starts Often the changes are not detected until the fever has subsided There is no parallelism between the severity of the tonsillitis or sore throat and the myocardial changes Occasionally a severe myocarditis develops in patients who have had only a few hours of fever sometimes they have not felt sufficiently ill to go to bed or else the tonsillitis was subclinical

Opinions are still divided on the incidence of myocarditis following tonsillitis According to some observers evidence of myocarditis is obtained electrocardiographically in 70 per cent of the cases This figure is certainly too high Marked changes consisting of widening of the QRS complexes to more than 0 10 second prolongation of the P—R interval abnormal RS T segment and abnormal T waves appeared in 30 per cent of another series (Hotz and Huber) According to personal experience 10 to 15 per cent of patients suffering from an acute tonsillitis develop changes suggestive of myocardial involvement

The patients complain of weakness palpitation and cardiac pain The pain may appear suddenly and without apparent provocation such as exertion it is felt behind the sternum or over the precordium it may radiate like the typical anginal pain to the right or left shoulder and arm Sometimes the distress is mild and is revealed only when the patient is specifically interrogated about it in other cases it is excruciating The pain may last only a few seconds rarely it persists for minutes and it recurs often

The signs are the same as those of other types of myocarditis and will be discussed later in this chapter

Often the lesion is overlooked The weakness and palpitation are attributed to the preceding infection or to the absorption of toxins Little attention is paid to the pain when it is atypical the patient is often young and therefore anginal pain is out of the question

The alterations in the electrocardiogram provide the best objective evidence of cardiac participation Temporary prolongation of the atrioventricular conduction time and periodically dropped beats (Wenckebach periods) may appear T wave changes are common These changes usually disappear in a few days rarely are they demonstrable for four to six weeks In some cases the conduction time remains prolonged even after full recovery takes place

Within the space of a few months the wives of two hospital administrators in the same institution complained of palpitation general weakness and cardiac pain following mild tonsillitis One patient had a temporary prolongation of the A V conduction time to 0 23 second and the other to 0 32 second Both women were young and otherwise healthy no subsequent evidence of rheumatic fever could be obtained and complete recovery was noted within two weeks

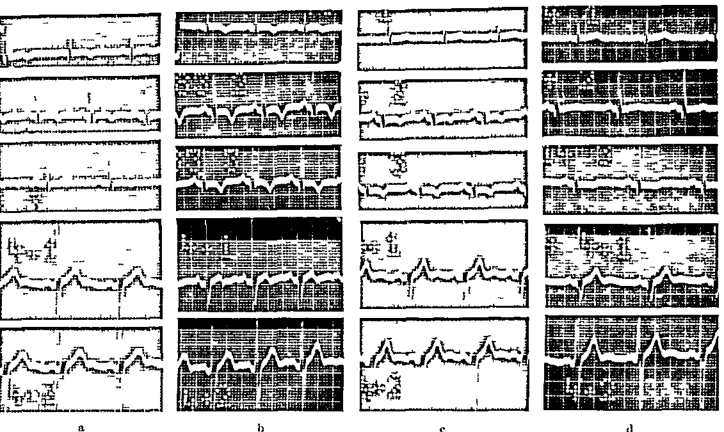


Fig 39 A series of tracings from a patient with myocarditis following tonsillitis The three standard leads are followed by CR4 and CR2

Figure 39 was obtained from a 25 year old man who came to the hospital with a severe tonsillitis and pharyngitis his temperature was 40° C Weakness and palpitation were the chief complaints Physical examination disclosed nothing abnormal except for the throat involvement Within five days the fever and tonsillitis subsided under sulphonamide therapy but the weakness and palpitation persisted for several weeks

The first electrocardiogram (figure 39 a) was taken on the second day of hospitalization The T waves are inverted in leads I and II The second electrocardiogram was recorded 6 days later one day after the fever disappeared It shows a sinus tachycardia of 100 and deeply inverted T waves in each limb lead The third tracing (figure 39 c) was obtained three weeks after the preceding and shows evidence of improvement The fourth tracing (figure 39 d) was obtained 18 days after the third and is almost normal The patient remained under observation and at no time presented evidence of rheumatic fever

Usually the prognosis is good because signs of cardiac involvement disappear within a few days or weeks We have never seen acute heart failure develop It is possible however that patients who are unaware of the existing condition may undertake severe exertion during the acute stage of myocardial involvement under these circumstances cardiac dilatation and congestive heart failure might develop Embolism of the systemic arteries may arise from mural cardiac thrombi but fortunately this is a rare event Little is known about any permanent weakness of the heart muscle due to scar formation following myocarditis (myocardial fibrosis)

The differential diagnosis is not always simple The process must be distinguished from rheumatic fever This is often difficult in view of the fact that arthralgias occur occasionally in connection with streptococcal infections of the upper respiratory tract Under these circumstances the sedimentation rate is of great help since it shows abnormal values for a long time in rheumatic fever but only a slight change for a few days after a streptococcal pharyngitis or tonsillitis Sometimes however differentiation of the two conditions is impossible in the beginning There is certainly an interrelation although the connections are understood only in part at present

Relatively little is known about the myocardial pathology since it is exceptional for these patients to succumb in the acute stage when a histologic study would be informative Available evidence however justifies the term myocarditis for the cardiac lesions It is of importance that most of the patients who succumbed to a simple streptococcic throat infection also had hyperthyroidism In a patient with mild hyperthyroidism who developed a complete heart block following tonsillitis an inflammatory lesion in the heart muscle particularly in the bundle of His contained gram positive bacteria (Davis and Smith) In experimental streptococcus infections in the rabbit inflammatory foci were seen in the myocardium for the most part around the small branches of the coronary arteries Therefore the possibility of an allergic response similar to that in rheumatic fever seems eliminated (Weicker and Petzlaff)

Penicillin should be given immediately 600 000 to 1 200 000 units being administered daily for several days Tonsillectomy should not be performed until six weeks after all signs of activity have disappeared Rest in bed is essential this must be enforced for days weeks or months in accordance with the clinical and electrocardiographic signs

Other Focal Infections These may likewise be accompanied by myocarditis Dental infections with or without focal abscesses or a tonsillar abscess are rarer causes of myocarditis than was formerly believed but such cases undoubtedly occur

An 18 year old man was admitted complaining of dyspnea and palpitation The heart was moderately enlarged and the sounds were pure A secondary anemia was present and the temperature underwent an occasional slight rise The electrocardiogram was repeatedly found normal until one examination disclosed a prolongation of the A V conduction time A renewed search for a focus of infection revealed a large latent apical abscess of one devitalized tooth Extraction of the offending tooth led to rapid and complete recovery of the patient

It is claimed that colitis cholecystitis adnexitis accessory sinus infections pyelitis and prostatitis may also act as foci and initiate a myocarditis in rare cases

Scarlet Fever Myocarditis is common in this disease Electrocardiographic alterations were found in 20 to 25 per cent of the cases observed Inflammatory changes likewise occur particularly around the small branches of the coronary arteries Histologic studies in scarlet fever and related streptococcal infections disclose focal and diffuse interstitial infiltrations in the myocardium in 90 per cent of the cases According to some authors rheumatic fever is superimposed in these cases whenever there are definite clinical signs of myocardial involvement

Coccal Infections Systemic diseases caused by staphylococci gonococci and meningococci often cause acute myocarditis as well as endo and pericarditis Modern treatment with the antibiotics permits a larger number of patients with these infections to survive and therefore more cases of myocarditis (and pericarditis) caused by these bacterial agents are observed

Parasites In trichiniasis the heart muscle is often involved and electrocardiographic changes are common They disappear soon and the parasite vanishes if the patient survives Focal myocarditis has been seen in toxoplasmosis (Paulley et al)

Syphilis Myocarditis is certainly rare in syphilis While it has been claimed that syphilis causes a diffuse chronic myocarditis and perhaps sudden death increasing doubt has been raised concerning the criteria for an anatomic diagnosis Spirochetes may abound in the myocardium of stillborn infants but inflammatory reactions are absent The importance of syphilis in the causation of coronary ostial stenosis and the resultant train of symptoms will be discussed later

Trypanosomiasis Chagas disease is known to cause myocardial lesions and cardiac arrhythmias Its high frequency in certain parts of South America has

been recognized lately (Rosenbaum and Mora) This disease may in the future assume importance in the United States

Tuberculosis Myocarditis although a common event in tuberculosis often is not evaluated correctly In our experience electrocardiographic changes are frequent in active exudative pulmonary tuberculosis and they are certainly not due to cachexia or avitaminosis since histologic examination of the e hearts shows definite changes due to tuberculosis

Four types of myocardial lesions are found in tuberculosis (1) the large solitary tubercle which may be as large as a fist and may be confused with a cardiac aneurysm (2) inflammatory infiltration of the myocardium which often starts from a tuberculous pericarditis (3) miliary nodules in the course of a generalized miliary tuberculosis (4) interstitial myocarditis (Gallavardin and Cravier) In one series tuberculous myocarditis was found in 10 of 100 cases of pulmonary tuberculosis (Roberts and Lisa)

Rather frequently we find abnormalities in the electrocardiograms of patients with an active exudative tuberculosis when they are examined prior to surgery thiamine deficiency atrophy or other degenerative diseases of the heart must be ruled out in such cases

Perrin et al described heart failure in young subjects caused by tuberculous lesions of the myocardium This etiology however is not proven in their patients

Typhoid Fever and Typhus Influenza Pneumonia Heart muscle involvement in typhoid fever consists largely of degenerative changes but actual inflammatory reactions are the rule in typhus As elsewhere in the body in typhus the inflammation is mainly in and around the vessels In uncomplicated influenza myocardial involvement is unusual but does occur occasionally It is common in pneumonia caused by pneumococci or streptococci

Virus Infections and Rickettsial Diseases The existence of myocardial changes in virus infections has often been demonstrated It appears in the experimental forms different viruses seem to evoke responses peculiar to the agent employed (Pearce) The myocardium may be affected in poliomyelitis In a series of 17 cases of poliomyelitis in which the heart was examined microscopically histologic evidence of myocarditis was found in ten (Saphir) The electrocardiogram was altered in 21 out of 52 patients with poliomyelitis (Frischknecht and Zellweger) and this was considered to be caused by potassium depletion This explanation may be valid for some of these changes Myocarditis appears in mumps Marked changes may appear in psittacosis In the course of an epidemic one of us had the opportunity to observe two physicians ill with psittacosis both had very marked but transient electrocardiographic changes The T waves were deeply inverted in lead I in one case and were inverted in all leads in the other

Electrocardiographic changes during life and perivascular infiltrations in the heart muscle after death have been seen in measles epidemic (viral) hepatitis primary atypical pneumonia infectious mononucleosis (figure 40) rubeola and influenza

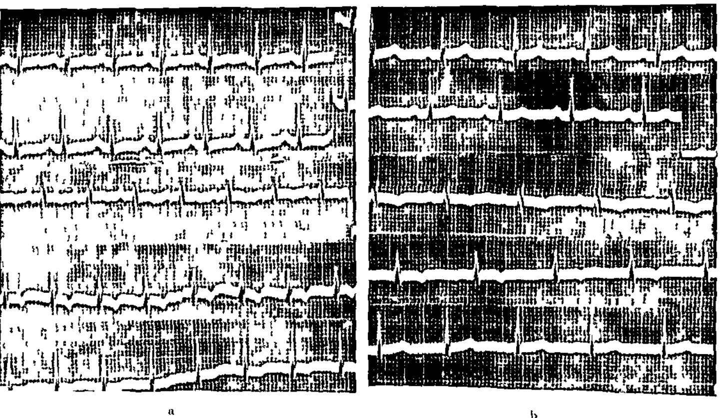


Fig 40 Abnormal T waves in the standard leads as well as in V 2 and V 5 in a 0 year old woman with infectious mononucleosis (a) Twelve days later (b) the electrocardiogram is normal

Cardiovascular lesions occurring in virus diseases have been reviewed by Lyon Rickettsial diseases scrub typhus for example occasionally cause a myocarditis

Acute Nephritis The nature of myocardial involvement in acute nephritis is still problematical but changes in the myocardium are the rule The importance of sudden cardiac failure in acute glomerular nephritis has been known since the classical work of Volhard *In a series of 138 cases clinical signs of cardiac damage* were found in 71 per cent Opinions are still divided on the question whether this is due to inflammatory reactions in the myocardium to toxic changes or to ischemia resulting from a generalized capillaritis with increased capillary permeability In the interstitial tissue exudate with cellular elements are found The venous pressure is increased in patients with acute nephritis (La Due) and hydrothorax is common (Zdansky)

Drug Allergy Of great interest are the changes occasionally seen after the administration of drugs Electrocardiographic changes followed the injection of arsphenamine (neosalvarsan) Histologic studies have revealed the occurrence of an eosinophilic myocarditis in patients under treatment with this drug Cardiac involvement appeared in one case after the seventh injection, and Charcot Leyden crystals and infiltrations of eosinophiles were found in the myocardium Some of these cases and others reported in the literature also developed a salvarsan dermatitis The mechanism is obviously one of idiosyncrasy or allergy

Every drug allergy and serum sickness may cause changes in the heart muscle resembling myocarditis with a necrotizing arteritis and periarteritis

A similar interstitial myocarditis with a rich infiltration composed of eosinophiles was described following the clinical and experimental use of sul phonamides These findings were denied by others (Fawcett) In all these in stances the heart was not exclusively affected but participated in alterations like the other organs

The possibility of allergic changes in the myocardium following the ad ministration of otherwise harmless drugs is established and this may prove a clue to understanding a very peculiar serious affection of the myocardium commonly called Fiedler s myocarditis

Postpartum Myocarditis Occasionally young women suddenly develop dyspnea tachycardia and edema 5 to 30 days postpartum The heart is found enlarged Mural thrombi may cause emboli in the systemic circulation (Sodeman) Severe focal inflammation of the myocardium is noted at post mortem The etiology of this syndrome is unknown and its differentiation from multiple embolisms from pelvic veins is difficult

Dermatomyositis The cardiac changes found in dermatomyositis a collagen disease of obscure origin are also unexplained

Fiedler s Myocarditis This lesion which has been called primary idio pathic acute interstitial isolated and pernicious myocarditis usually affects young adults *However it also occurs in children and apparently* is not as rare as the few cases reported in the literature would seem to indicate

Grossly the heart may show hypertrophy that may attain considerable proportions The ventricles are involved more than the atria and the left ventricle more often than the right The inner layers of the myocardium usually suffer more than the outer ones *The parenchyma itself is only slightly involved In* one type there is extreme infiltration with various types of white blood cells sometimes mainly eosinophiles In the second type the lesion is granulomatous *with fibroblasts and giant cells but tuberculosis is not responsible*

Usually the onset is abrupt and ordinarily the course is one of progressive cardiac failure Fever chills lassitude and anxiety may characterize the onset Two of Saphir s 13 cases died suddenly and some of them had anginal pain Percussion usually reveals cardiac enlargement Ordinarily tachycardia and hypotension prevail The cardiac sounds are often altered and gallop rhythm is frequent The electrocardiographic changes if present are consistent with a diffuse myocardial lesion The disease is fatal within a period of days a few weeks or rarely months Pulmonary and cerebral embolism are frequent

Treatment to date has been futile the fatal outcome seeming to justify the term pernicious myocarditis (Boikan)

The terms essential idiopathic and isolated myocarditis indicate that the heart alone is affected insofar as postmortem studies show The etiology of the disease is unknown Since some other types of myocarditis are definitely allergic *the same possibility must be seriously entertained in the pathogenesis of Fiedler s* myocarditis It is also uncertain whether the disease is invariably fatal and what if any is its relation to milder forms of myocarditis The relation of Fiedler s myocarditis to the myocardial lesions of avitaminosis will be discussed later in this chapter

The Clinical Picture of Myocarditis

With certain readily understood exceptions dependent upon the etiology and accompanying disease the subjective symptoms and objective signs in all cases of myocarditis are similar Some of them were mentioned in the discussion of tonsillitis (p 250)

Symptoms The subjective symptoms are usually mild and not characteristic Palpitation is frequent and sometimes annoying General weakness is pronounced Anorexia and loss of weight are often noted

Precordial pain is a very common symptom appearing without provocation and lasting only a few minutes The pain may be very intense and may radiate *to the shoulders and arms*

In most cases the above mentioned complaints are not sufficiently striking to draw the attention of an unwary physician to the heart

Signs The paucity of physical signs is explained by the fact that inflammatory foci scattered diffusely in the heart muscle usually do not alter cardiac size or auscultatory phenomena Only the rare more extensive inflammations produce changes detectable by percussion or auscultation

Fever is common in the acute stage but is often first noted by the physician because the patient is unaware of it While the temperature may exceed 38 5° C it may be absent even in a florid myocarditis

Cardiac enlargement is absent or minimal in an otherwise healthy heart but in some instances particularly when the patient does not remain in bed the enlargement may be pronounced Nevertheless this enlargement is usually *transient in contrast to the persistent form encountered in rheumatic valvular* lesions moreover it recedes with striking rapidity

When a decompensated valvular defect with an enlarged heart is successfully treated and compensation is fully restored cardiac size usually remains constant If cardiac size diminishes during treatment it is assumed — correctly in our experience — that a pericardial effusion was present and has now decreased or disappeared However cardiac enlargement may recede considerably in myocarditis

Fluoroscopy often reveals very strong pulsations and marked excursions of the cardiac border Cardiac dilatation is often absent when the patient is examined by x ray in the upright position but is detected in the supine position (Zdansky) This is explained by the increased return of blood to the heart resulting in greater filling of the cardiac chambers in the recumbent position

Auscultation often reveals normal pure heart sounds The heart rate is fast and accelerates markedly even on slight exertion but this sign is not always present A systolic apical murmur if present is not characteristic The first or second sound is often split In severe myocardial lesions the heart sounds become distant and impure Gallop rhythm is often present Arrhythmias due to partial A V block are not rare but extrasystoles are rather unusual A progressive anemia occurs in many protracted cases

The electrocardiogram reflects the involvement of the myocardium more often than any other method of examination Alterations are not always evident and are not continuously present even in proven cases They develop only when inflammatory foci exist at definite places in the specific tissue or when large foci are situated in definite areas of the myocardium Since new foci constantly light up and vanish the electrocardiographic changes consisting of widened *QRS* complexes abnormal T waves and conduction disturbances may be present one day and gone the next Frequent electrocardiograms are necessary and one positive record will establish the diagnosis

Diagnosis If the diagnosis of myocarditis were suspected more frequently it would be more widely appreciated that the affected patients need not manifest symptoms or signs demonstrable by percussion auscultation x ray or even electrocardiography Therefore if patients were examined more often with this diagnosis in mind the lesion would be found in innumerable cases currently unrecognized

Since these patients *must rest in bed and must avoid every unnecessary* demand upon the heart timely recognition is of utmost importance

Probably the connective tissue scars discovered so frequently by pathologists in the heart muscle (fibrosis of the myocardium) in patients dying for diverse reasons but without coronary artery diseases are often due to an old healed myocarditis In view of the frequency of infections and the realization of the incidence of myocardial participation even in mild infections the assertions made in earlier editions of this book should be repeated namely that we believe that only a few individuals entirely escape the occasional presence of small inflammatory foci in the myocardium (myocarditis)

Complications As previously suggested one of the most serious nonpreventable complications is a peripheral embolus originating from a mural thrombus In some young hemiplegics who have no signs of lues or a congenital aneurysm an undiagnosed myocarditis explains the accident

Abscesses form in *overwhelming sepsis subacute bacterial endocarditis* and myocardial infarction Such an abscess may perforate outwardly Cardiac aneurysms sometimes develop

Prognosis In most cases prognosis is excellent and healing of the lesion is thorough Only in a minority of cases most of them at present still included in the group called Fiedler s myocarditis is the outcome fatal The course of the disease in such cases may be rapid with early death

Treatment Bed rest the eradication of focal infection and antibiotic drugs are the only methods of treatment available If allergy toward a drug is discovered its administration should be discontinued Rest in bed should be enforced as long as electrocardiographic changes fever tachycardia or changes in the character of the heart sounds indicate activity of the myocarditis In infectious myocarditis antibiotics should be given in sufficient doses In the allergic type it is often difficult to find the responsible antigen

MYOCARDIAL DEGENERATION

The diagnosis of myocardial degeneration is justified only if an etiologic factor is detected The myocardium like any other muscle does not degenerate without some extrinsic cause At one time myocardial degeneration was diagnosed in every cardiac patient who did not have a valvular lesion

Cardiac Atrophy

Atrophic changes of the myocardial fibers constitute the most common change in the heart There is rarely a severe wasting disease (tuberculosis a malignant tumor severe anemia or a prolonged debilitating disease) that is not associated with cardiac atrophy These hearts are firm because the connective tissue does not share in the atrophy to a comparable degree the coronary arteries may become tortuous since they also escape atrophy Apart from this simple atrophy brown atrophy is also encountered especially in older individuals These atrophic hearts usually are capable of meeting the demands imposed upon

them by individuals whose activities are necessarily limited although there is a definite decrease in the reserve power

Some of these hearts weigh less than 100 grams Often there is a bradycardia particularly in hunger atrophy The blood pressure falls and the electrocardiogram shows low voltage due to loss of muscular substance

Cloudy Swelling

Among the degenerations in a more strict sense there is the cloudy swelling which accompanies a host of infectious diseases and which may result from intoxications with chloroform as well as many other agents The cardiac involvement is a single example of a widespread process with similar lesions in other parenchymatous organs

Grossly the flabby heart looks like boiled muscle

Diphtheria

An outstanding instance of myocardial degeneration is the involvement of the muscle in diphtheria which too often is called a myocarditis Actually reactive inflammatory processes occur secondarily, like those at the border of a myocardial infarct after coronary occlusion The primary lesion of the heart in diphtheria is a focal degeneration and necrosis of the muscle fibers later a reactive inflammation and proliferation of the fixed tissue cells appear These changes have a toxic origin they are often widespread and the prognosis may be serious Nowhere is the recuperative power of the heart more clearly manifested than in diphtheria If patients survive the acute phase cardiac failure soon disappears a complete atrioventricular block or bundle branch block vanishes and after a few months the patient may present normal cardiac findings This is one of the reasons it was formerly held that the acute cardiac failure was primarily of the peripheral circulatory type that is vasomotor rather than cardiac In rare cases atrioventricular block or bundle branch block persist (Hoel and Perg)

The clinical picture is well known There is hardly a more tragic experience *than that of observing a child pass through diphtheria and suddenly succumb* to a cardiac affection The premonitory symptoms are few in number and often elude detection When present they consist of vague precordial oppression dyspnea and palpitation General weakness is often noted Epigastric pain and vomiting may usher in the acute syndrome and death may occur in a lapse of consciousness Extreme pallor is present Usually there is no fever Often sinus tachycardia partial or complete heart block are observed Extrasystoles are rare The presence of conduction disturbance is considered particularly ominous Even if sudden death does not occur early the final outcome may be dubious for weeks A considerable number of these cases recover and have no permanent sequelae

There is no specific treatment once the myocardial damage develops Bed rest must be strictly enforced for weeks since slight exertion has been known to cause sudden failure Otherwise treatment is symptomatic

Fatty Degeneration in Anemia

This alteration of the heart muscle seems to be provoked by the same causes as those responsible for cloudy swelling the causative factor apparently acts over a long period of time and more intensely This lesion played an important role in medicine up to a few decades ago At present however it is rather uncommon since the modern treatment of anemias has found universal use for it was in this group of conditions that fatty degeneration attained clinical importance This degeneration often involves the entire heart particularly the subendocardial layers causing the picture of the tiger heart Alterations are usually most evident in the right ventricle especially around the papillary muscles Cardiac enlargement and murmurs appear The enlargement is due to dilatation of both ventricles and congestive heart failure (predominantly right heart failure) may follow With cardiac dilatation and the acceleration of blood flow consequent to the anemia systolic and occasionally diastolic murmurs become audible and very often lead to the erroneous diagnosis of a rheumatic valvular lesion The cardiac output becomes elevated when the hemoglobin level falls to 7 Gm per 100 ml of blood There is a reduced blood volume in anemia and peripheral arteriolar dilatation The circulation time is abnormally short

While relative mitral (and *even relative aortic) regurgitation* occurs the systolic and diastolic murmurs in these patients usually arise from the veins near the heart and are the result of the increased speed of blood flow

Fat Infiltration

This is a rare lesion in obese individuals Not only is the subepicardial fat increased but true infiltration occurs in the myocardium This condition is also more common in the right ventricle Owing to the fact that small interstitial cells when they become fat cells have an increased size the myocardial fibers are pushed apart an event which is important when *the thin wall of the right* ventricle is extensively permeated by fat cells When fat infiltration is moderate it seems to lack functional significance When extreme (a rather rare occurrence) it may produce right heart failure and even death by rupture of the right ventricle (Smith and Willius)

Thiamine Deficiency (Beriberi)

Cardiovascular involvement as the result of nutritional disturbances have been studied for many years The type following thiamine deficiency was observed first in East Asia and in the East Indies

Incidence Cases of beriberi due to nutritional disturbances are observed in the Western Hemisphere relatively often They are found in alcoholics drug

addicts pregnant women and individuals who voluntarily (faddists) or on medical advice follow special diets These individuals frequently develop severe cardiac changes from avitaminosis Many patients of this kind may be seen in a hospital ward each year *Even on a normal diet cardiac damage may result from an* abnormal absorption or an abnormal utilization of thiamine

Mechanism Lack of thiamine disturbs tissue oxidation The amount of tissue cocarboxylase is diminished Pyruvic acid and lactic acid are not broken down and are found in the blood in larger quantities In thiamine deficiency Raab found an excessive accumulation of adrenosympathetic substances in the heart muscle which may explain the short P P interval in the electrocardiogram

Symptoms and Signs Besides general weakness the usual symptoms of heart failure — dyspnea on exertion swelling of the ankles and palpitation — are present

Examination reveals a collapsible pulse which may resemble the Corrigan pulse of aortic insufficiency The diastolic blood pressure is low a systolic sound is heard over the peripheral arteries and a capillary pulse is present These phenomena are at least in part due to a general peripheral vasodilatation The *signs are more pronounced in the oriental type of beriberi but are not completely* absent in the occidental form (Aalsmeer)

Usually the heart rate is increased The heart is diffusely enlarged particularly to the right the pulmonic arc is prominent Evidence of right (and left) heart failure occurs Palpation reveals marked hypermotility of the cardiac area This may be connected with the greater amounts of adrenalin and related compounds which have been found in the heart muscle of rats in vitamin B_1 deficiency (Raab and Suplee)

The heart sounds are often impure Gallop rhythm may appear but arrhythmias are rare The blood pressure is often low and the velocity of blood flow is increased

The patient may show other evidence of vitamin deficiency In tropical beriberi electrocardiographic alterations are infrequent Apart from a relatively short P I interval little has been found even when marked cardiac dilatation and congestion prevailed Definite depression of the RS T segment and T wave changes were described in occidental beriberi and in our experience they are common (figure 41) Occasionally the P R interval is prolonged and the QRS complexes are widened The discrepancy between the electrocardiographic findings in oriental and occidental beriberi does not seem to have been explained In all probability the lack of other vitamins plays a role While in oriental beriberi right ventricular failure with right outflow tract dilatation is common it is rare in the occidental type

Pathology Hydropic degeneration of the myocardium originally seemed to explain the severe myocardial lesion The water content of the heart muscle however is not increased in experimental beriberi In recent years focal myocardial necrosis has been found in avian and mammalian hearts during thiamine deficiency The necrosis is often visible to the naked eye Just as in other local

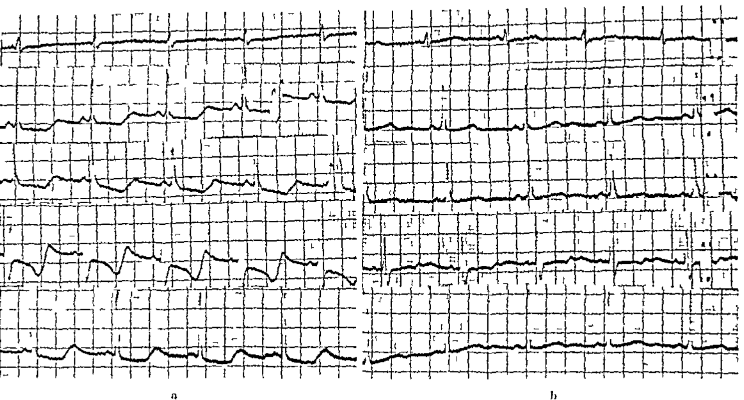


FIG. 41. An electrocardiogram in the standard leads as well as in V_2 and V_5 of a 49 year old woman suffering from alcoholism. The P-R intervals measure 0.11 second and the RS-T segments and the T waves are abnormal (a). After a week, during which thiamine chloride was given, the electrocardiogram (b) was almost normal.

degenerations the necrotic area may be secondarily infiltrated with leukocytes scars form during healing Sometimes the endocardium becomes thick and the *resulting mural thrombi may cause embolism* The histologic changes may closely resemble those seen in Fiedler s myocarditis For these reasons the question has even been raised whether individuals supposedly suffering from idiopathic or essential myocarditis did not in reality have a thiamine deficiency (Dock)

It is possible that further investigation will show that allergic and nutritional disturbances explain many of the hitherto puzzling cases of essential myo cardial lesions It is evident furthermore that nutritional disturbances in cardiac patients may damage the heart and aggravate existing conditions Inadequate nutrition is common in patients with chronic cardiac disease

Therapy The degree of myocardial necrosis and reactive inflammation may explain why the administration of large doses of thiamine chloride (100 to 150 mg daily) to some patients with a beriberi heart leads to rapid recovery while in others prolonged treatment is necessary Clearly hearts in which anatomic changes have already appeared require a longer time for recovery If the heart *muscle has been irretrievably damaged improvement becomes impossible*

When there are disturbances of absorption large doses of thiamine chloride must be given parenterally for a longer time than in cases of thiamine deficiency due to lack of intake The absence of cheliosis of abnormal reflexes and of tongue changes does not speak against the diagnosis A deficiency of other components of the vitamin B complex need not be present

Other Types of Degeneration

Myocardial Lesions Caused by Disturbances of the Electrolyte Balance We are only *now beginning to understand the disturbances of the myocardium* caused by abnormal electrolyte content of the blood and heart muscle The disturbances of potassium content are known best since they cause electro cardiographic as well as histologic changes in the heart muscle

In patients with a great variety of lesions hypopotassemia or hypokalemia can develop It is seen in chronic diarrhea particularly in infants in diabetic acidosis in sprue after surgical operations following the administration of desoxycorticosterone or cortisone and in aldosteronism The changes may be particularly striking after the intravenous injection of glucose indeed such therapy may be dangerous in patients with the above mentioned conditions

The patient may experience dyspnea Cardiac enlargement is found Irregular rhythms interference between sinus and A V rhythms and extrasystoles appear

Histologically in animal experiments (pig rat) and in man (McAllen) pin point necrosis of myocardial fibers with infiltration by polymorphonuclears and bands of *fibrotic tissue are seen* Similar lesions (*interstitial myocarditis*) (Keye) have been reported in Friedreich s ataxia scleroderma and progressive muscular dystrophy It is of interest that in rats the myocardial necroses which appear on a potassium low diet are prevented by thiamine deficiency (Follis)

The electrocardiographic changes consist of a depression of the PS T segment and very prominent U waves (Bellet) An accompanying prolongation of the Q T interval is caused by a hypocalcemia present at the same time It is not yet decided whether the electrocardiographic changes are more related to the serum

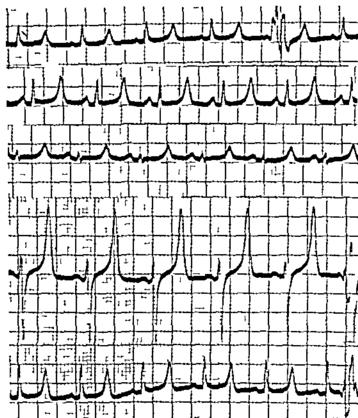


FIG. 49 The electrocardiogram of a 34 year old woman with acute renal failure and hyperpotassemia (6 mEq) The T waves in the standard leads as well as in V 2 and V 5 are abnormally high and tent like They have a small base and the ascent and descent are almost symmetrical

than to the myocardial potassium level In congestive cardiac failure and in a variety of myocardial diseases the K content of the myocardium is diminished Large doses of digitalis have the same effect In some patients with large myocardial infarctions the potassium level in the blood rises

Hyperkalemia as seen in azotemia Addison s disease or in untreated diabetic acidosis great muscular weakness and mental confusion may appear The electrocardiogram shows typically huge T waves with small bases peaked reaching sometimes the height of the P waves With rising levels of potassium intraventricular block arrhythmias and atrial paralysis appear

Figure 42 shows the electrocardiogram in a moderate figure 43 in an advanced hyperkalemia Figure 44 shows patterns of hypo and hyperkalemia in the same patient

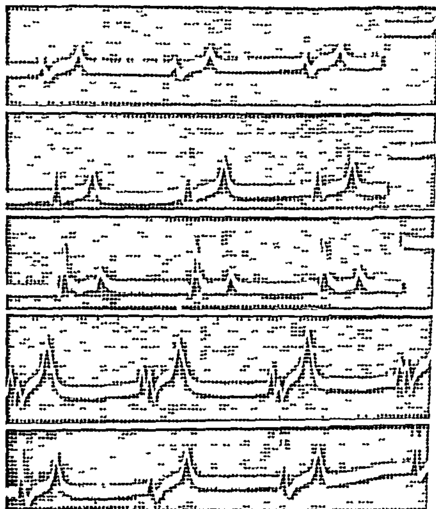


FIG 43 Pattern of hyperpotassemia in a patient with chronic nephritis and renal failure The T waves show a similar pattern to that in figure 42 the QRS complexes are slurred and widened and the sinus rhythm is replaced by an atrioventricular rhythm

Other Types Several degenerative processes in the heart muscle e g those caused by hypothyroidism or toxic doses of digitalis will be discussed under appropriate headings but a few others may be noted at this time Simple hyaline degeneration may occur in the interstitial tissue and in the blood vessels Zenker s hyaline degeneration with swelling and rupture of the fibers occurs in typhoid fever when massive this form of coagulation necrosis may cause circulatory disturbances

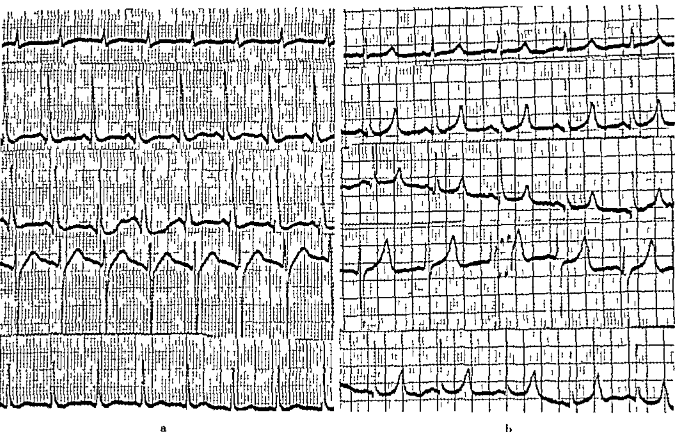


FIG. 44. A 26 year old woman had a cholecystectomy with prolonged drainage. The electrocardiogram shows the pattern of hypokalemia with depressed RS-T segments and absent T waves (a). Hyperkalemia developed (b) after too energetic therapy.

As a mesoblastic structure the heart may also suffer from primary as well as secondary amyloidosis In primary systemic amyloidosis the heart is involved in 80 per cent of the cases The clinical picture may simulate pericardial adhesions As in other degenerative cardiac diseases only T wave changes are visible in the electrocardiogram Primary cardiac amyloidosis occurs most often in the elderly patients The diagnosis is usually missed since coronary sclerosis is suspected

Myocardial damage due to trauma or caused by physical agents (x ray) will be discussed in a later chapter

Degenerations of Unknown Etiology During the last war Bedford and Konstam described a severe myocardial disease in West Africans that affects young people and is of unknown etiology Signs of heart failure with dyspnea and edema suddenly appear general weakness is pronounced and the blood pressure is low Subendocardial necrosis is found and strands of fibrotic tissue are present in the myocardium Mural thrombi are common Rarely there is an eosinophile reaction A deficient diet was considered as etiologic and prolonged malnutrition was actually found to induce similar changes (Toreson) Subsequently it was noted that the histologic changes are different from those seen in beriberi Furthermore, the illness certainly occurs without malnutrition Cray found the syndrome in two Europeans who had visited West Africa The possibility of a virus infection has been discussed

The disease has also been observed in the United States (McKusick and Cochran)

Clinically these patients are admitted with evidence of congestive heart failure Relative mitral and tricuspid insufficiency caused by involvement of the papillary muscles and thickening of the valves leads to the wrong diagnosis of a rheumatic valvular lesion Men are affected more often than women The clinical picture may simulate that resulting from pericardial adhesions with constriction of the heart (Loeffler) The situation rapidly deteriorates and there is no response to therapy

This syndrome is probably related to the syndrome described by Loeffler in which there is endocardial fibrosis with thrombosis and eosinophilia It may also be noted that after experimental stress Selye found similar strands of fibrotic tissue in the myocardium as a sign of his general adaptation syndrome

Also of unknown mechanism are the myocardial changes frequently seen in Friedreich s ataxia progressive muscular atrophy and myotonia atrophica In the latter condition an abnormal electrocardiogram was found in 68 3 per cent of the cases Bundle branch block and atrioventricular block are common

Paget s Disease Involvement of the circulation is common in Paget s disease Paget himself described the increased blood supply to the involved bone with increased warmth over the involved area With widespread involvement of the bones the cardiac output was reported as amounting to 13 3 liters per minute in one case (Edholm et al) In addition such patients often have hypertension and an increased *incidence* of atherosclerosis Kyphoscoliosis is common and may

contribute to the circulatory embarrassment Lequime and Denolin found at rest no increase of circulation it appeared however following exercise provided abnormality of the bone was widespread

CORONARY SCLEROSIS

Introduction

Atheroma is a lesion caused by lipid deposits in the intima In atherosclerosis *in addition to such deposition there is a proliferation of the intima and calcium* deposits may appear Arteriosclerosis is in itself not an entity three main types of arteriosclerotic processes being distinguished at present

(1) *Monckeberg s Sclerosis* Medial calcification of the arteries Monckeberg s sclerosis is *a more or less physiologic phenomenon Small deposits of lime salts* appear very early in the media of human arteries particularly in the pelvic vessel They are a regular finding in patients beyond the age of twenty (Clawson) and are more common in males than in females When this process is somewhat more pronounced it is referred to as Monckeberg s sclerosis It occurs most often in the femoral pelvic radial and temporal arteries it is rare in the coronary arteries The lack of cholesterol deposits in the intima distinguishes this process from true arteriosclerosis but the two lesions may be combined Since medial sclerosis does not narrow the arterial lumen it ordinarily has no clinical significance The small calcified areas may be present as nodules or more commonly as rings and give rise to so called corduroy arteries If these rings fuse in continuous calcification pipestem arteries will be felt when the peripheral arteries are palpated

Physicians should be aware of the great incidence of this process since patients sometimes become very apprehensive when lime salt deposits are found in the arteries of the abdomen the pelvis or the extremities on the occasion of an x ray examination performed for some other reason

A similar process can be produced in animals by injections of epinephrine by overdosage with vitamin D and by prolonged radiation with ultra violet light *Examples of medial calcification in the newborn have been described*

(2) *Arteriolosclerosis* A second type of arteriosclerosis is more accurately des*cribed as arteriolosclerosis The term is applied to the arteriolar involvement* that occurs in hypertension It does not seem to depend upon the age of the patient Its relation to the third type is not clear Arteriolosclerosis will be discussed in association with hypertension

(3) *Atherosclerosis* Atherosclerosis is the chief cause of coronary artery pathology The following pages are devoted to this type of arteriosclerotic process

Atherosclerosis — Pathology

The lesion is seen in early youth The milk streaks in the aorta are due to the presence of foam cells in the intima They are found in most children over 8 years of age The mitral valve is affected particularly often at times even in

infancy (Aschoff Hirsch) The high cholesterol content of the food at this age may be responsible Lipid substances deposited in the intima of arteries and valves in early childhood are readily absorbed but the capacity for reabsorption disappears in later years The atheromatous plaques become larger and reabsorption does not take place

In children the atheromatous plaques are situated within the intima The plaques contain — as does the blood — cholesterol cholesterol esters phospholipids and dihydrocholesterol Later on beginning with the third decade they are more prominent and narrow the lumen of the artery since intimal proliferation becomes more pronounced

The left coronary artery is involved earlier and more often than the right (108 times out of 120 cases) The process is more common near the origin of the coronary artery Lime salts are deposited later Thin walled capillaries grow into the athero sclerotic area from the adventitia and the lumen of the artery when the subject reaches the fourth decade (Wolkoff) The importance of these vessels for the devel opment of coronary thrombosis will be discussed in a later chapter

White plaques of lipid deposits appear in the aorta and valves in infants they are present in the main coronary arteries in patients 18 to 20 years old In subjects over 30 the chief branches are involved and between 50 and 60 fibrous prominent plaques which may obstruct the lumen are found also in the smaller tertiary branches of the coronary tree (Wolkoff)

Thickening of the intima is a physiologic process characteristic for the coro nary arteries (Dock) In patients between 40 and 50 years of age the thickness of the intima of otherwise normal coronary arteries may surpass the thickness of the media (Wolkoff) This is less pronounced in women

Etiology

Lipid Metabolism Since the classical experiments of Anitschkow which demonstrated the increased incidence of atheromatosis in rabbits fed large amounts of cholesterol new data have been obtained regarding the relation of lipid metabolism to atherosclerosis Nevertheless the problem is far from solved

Little is known about cholesterol metabolism It is certain that cholesterol can be formed in the body by building stones as simple as acetate derived from carbohydrates fats or proteins But the transport the regulation of cholesterol levels and details of its function in the body are unknown According to Certler et al the values of the different lipids in the blood are higher in mesomorphic individuals Lower levels of serum lipids were found in normal individuals aged 80 to 100 years old if compared to middle aged persons (Goldbloom and Fiber)

With regard to the absolute level of cholesterol and cholesterol esters it is certain that normal levels may be found in patients with severe atherosclerosis while high abnormal levels are seen without it However the following laboratory findings are obtained in most patients with atherosclerosis

THE CHOLESTEROL PHOSPHOLIPID RATIO In addition to cholesterol the phospholipids of the blood represented for the most part by lecithin are of

importance They act as stabilizers of the cholesterol protein molecules Even a marked elevation of the serum cholesterol often does not lead to atherosclerosis when the cholesterol phospholipid ratio is normal that is when the phospholipids are also present in larger amounts and in their normal relation to cholesterol Thus in familial hypercholesterolemia the phospholipids are not increased the cholesterol phospholipid ratio is high and atherosclerosis is common on the other hand the latter disease is rare in idiopathic hyperlipemia because here the phospholipids are also increased

THE BETA LIPOPROTEINS *The cholesterol molecules are not free in the serum* but like the phospholipids they are combined with giant protein molecules These molecules called lipoproteins consist of alpha lipoproteins the protein molecules being derived from alpha globulins and the beta lipoproteins derived from beta globulin The total cholesterol in the alpha lipoproteins is diminished but it is increased (70 per cent) in the beta lipoproteins in patients with atherosclerosis

PHYSICAL CHARACTERISTICS OF THE LIPIDS With the ultracentrifuge Gofman and his co workers found lipoproteins of different sizes and densities These large molecules float at different levels with a certain speed of the ultracentrifuge and are classified according to Sf (Svedberg flotation) units Molecules which flotate within a range of Sf 10 to 20 and Sf 20 to 100 units were found to be important in relation to atherosclerosis Feeding a cholesterol and fat rich diet increases the amount of these molecules a diet free of fat and cholesterol diminishes their amount in the blood Among patients with myocardial infarction 91 per cent are said to possess a larger number of these molecules in the serum there is a particularly strong association between atherosclerosis and levels of Sf 10 to 20

The relation between atheromatosis of the coronary arteries and the Sf levels is said to be better than that of the cholesterol values While some confirmation of this statement is available additional data must be collected before further conclusions are drawn It must be emphasized that in the individual case all the values mentioned above may be normal and advanced coronary sclerosis can exist however when groups are studied the abnormal values are prevalent

HYPERCHOLESTEROLEMIA AND CORONARY SCLEROSIS Diseases associated with large amonts of lipid (cholesterol) in the blood have a proclivity for the development of atherosclerosis and coronary sclerosis in particular as a complication Thus these processes complicate hypothyroidism rather regularly

In diabetes the disturbance of carbohydrate metabolism is usually associated with altered fat metabolism and coronary as well as general atherosclerosis appear more often than in the general population moreover these lesions appear at an earlier age Since the introduction of insulin diabetic coma has become rare and atherosclerotic cardiovascular disease has become the most common cause of death in diabetics It has been estimated that more than 90 per cent of diabetics whose disease has lasted more than ten years have generalized atherosclerosis

a low caloric fat poor high carbohydrate diet has been recommended to prevent this arterial lesion While the evidence at hand is not sufficient to prove that diabetes can initiate atherosclerosis there is no doubt that in diabetes the vascular atherosclerotic changes are augmented and accelerated While some believe that careful control of the diabetes can prevent atherosclerosis (Joslin Dunlop) others deny this

Atherosclerosis has been described in nephrosis (Weiss and Minot) The disorder is also common and hereditary in some types of xanthomatosis (e g Hand Christian Schuller disease) which are associated with a high blood cholesterol In certain types of obesity or cholelithiasis coronary sclerosis is common Statistical investigations indicate that diets containing excessive amounts of fat favor the appearance of atherosclerosis

Atheromatosis of the aorta the result of cholesterol feeding is accelerated in experimental animals by castration thyroidectomy and the administration of posterior pituitary extracts Administration of iodine compounds prevents the appearance of atherosclerosis induced by feeding cholesterol in rabbits

The investigations of Bronte Stewart et al are important because they confirm the finding that in general the higher the economic level of their patients the higher the serum cholesterol There was a close correlation between intake of fats and the cholesterol level The protein intake did not influence the results Olive oil and different fats with a high content of unsaturated fatty acids depress the serum cholesterol level So does cottonseed corn oil and soy bean oil (Kinsell et al)

Unsaturated fatty acids are those which have double bonds in the carbon chain The degree of unsaturation is measured by their iodine number The essential fatty acids (oleic acid linoleic acid and arachidonic acid) prevent lipemia after ingestion of fats and eggs and depress the beta phospholipids in the blood

Pyridoxin Deficiency of vitamin B_6 causes in monkeys a lesion similar to human atherosclerosis (Rinehart and Greenberg) Pyridoxin is involved in the formation of unsaturated fatty acids (Schroeder) The intake of 6 mg of pyridoxin daily has been recommended for prophylactic reasons

Lesions of the Intima According to some the deposition of lipoids (cholesterol esters) is the primary factors whereas others believe that some lesion of the arterial intima represents the primary alteration Abnormal metabolism of the tissues and abnormal enzyme function have also been considered

Inflammation The part played by inflammation is illustrated best by syphilitic aortitis where secondary atheromatosis is common The appearance of atherosclerosis as a consequence of other kinds of arteritis is often discussed but remains unproven Duguid believes that nonoccluding thrombus formation in the arterial intima leads to a picture resembling atherosclerosis

Mechanical Factors These seem to play an important role The atherosclerotic changes in the heart valves appear at places exposed to the greatest

mechanical strain these are the aortic surface of the aortic valves and the ventricular surface of the mitral valves Atherosclerotic processes are also more frequent at the bifurcation of arteries Even trauma seems to play some part in the development of local atherosclerosis

Hypertension likewise seems to be a factor Coronary sclerosis was found in 20 per cent of the hypertensive subjects in a series of 4678 autopsies while it was present in only 6 2 per cent of those with normal blood pressure Hypertension seems to be an accentuating and accelerating factor rather than a causal one in atherosclerosis

Atherosclerosis is common in the lesser circuit in conditions in which the pressure is high e g cor pulmonale and congenital heart disease

Adiposity An increased incidence of atherosclerosis in the obese is often stressed but occasionally is denied The denials are particularly concerned with a lack of greater incidence in women

Tobacco The relation of smoking to the occurrence of coronary sclerosis is not fully elucidated Many assume the incidence of coronary sclerosis is increased in heavy smokers Some believe that an increased output of epinephrine under the influence of nicotine is responsible for the coronary sclerosis of smokers Statistics showing that tobacco shortens the duration of life were found to be more significant as the amount of consumed tobacco increases (Pearl)

It is certain that nicotine may induce functional narrowing of peripheral vessels but whether this will cause atherosclerosis is still undecided

Other Factors It is interesting that ultraviolet irradiation of cholesterol and egg yolk inhibits their atherogenic property experimentally (Altschul) Alloxan diabetes in rabbits does not lead to atherosclerosis and even prevents this lesion following cholesterol feeding However the phospholipids are markedly increased in these conditions

Sex

There is a distinct difference in the incidence of coronary sclerosis in the two sexes — the disorder is much less common in younger women unless they suffer from hypertension or diabetes

In patients under 40 years of age the disease is much more common in men After 60 years the incidence is the same in both sexes This relation has often been attributed to the influence of the sex hormones Recent experiments showing the prevention of atherosclerosis by estrogen therapy serve as a confirmation The degree of atherosclerosis in women with bilateral oophorectomy is greater than in women in general (Wuest et al) Estrogen seems to clear the plasma of high molecular lipids Estrogens correct pathologic protein lipid relationship Hypogonadism in both sexes is associated with an increase of alpha lipoproteins they are increased by stilbestrol and reduced by methyl testosterone

Coronary sclerosis begins earlier in males The peak of incidence is reached between 55 and 59 In women the rise is slow from the ages of 40 to 70 years (Peel)

Even in men the oral administration of estrogens tends to correct pathologic protein lipid relationships of the survivors of myocardial infarction Methyl testosterone has an opposite effect (Russ Eder and Barr) The mechanism of this action is unknown

Race Eating Habits

A racial factor has been postulated for there is some evidence to suggest that coronary sclerosis is particularly common in Jews and relatively infrequent in Negroes It seems however that it is not the race but the dietary habits that are responsible There is no doubt that Negroes in Africa and Chinese in China have less atherosclerosis but show the same incidence as soon as they adopt American eating habits In areas of the world where little fat is consumed investigations show a lesser incidence of hypercholesterolemia and of atherosclerosis

Dramatic proof of this situation was provided during the war In Finland Norway and Sweden the incidence of deaths due to atherosclerosis fell during the war when the consumption of fat was diminished and rose again with the resumption of customary eating habits In Denmark where fat consumption rose during the Second World War the opposite trend of mortality due to heart disease as the result of atheromatosis occurred (Malmros Strom and Jensen)

Kuczynski s investigations on the nomads of the Kirgiz steppe where the mortality among young males from coronary disease was tremendous are well known The food consisted chiefly of large quantities of mare s milk and its products

One has to consider that with diminished consumption of fat the intake of proteins also is often diminished The diet too is frequently undercaloric

Age Heredity

Coronary sclerosis is definitely not a disease of any particular age for it occurs in young people and it may be absent in the aged Occasionally marked coronary sclerosis and even coronary thrombosis is seen in infants it has also been found in siblings (Menten and Fetterman)

It is astonishing how frequently patients with coronary sclerosis reveal that the same lesion is present in other members of the family We have observed one family in which one brother died of coronary sclerosis at 46 another developed left ventricular failure gallop rhythm and marked changes in the electrocardiogram due to coronary sclerosis at 45 a third brother had a coronary thrombosis at 50 and a fourth brother was discovered to have hypertension when he was 42 Heart block due to coronary sclerosis has been observed to develop in twins at approximately the same time and an involvement of the same artery must be assumed Abnormal cholesterol metabolism is also hereditary

It is important to note that coronary sclerosis may be found without evidence of atherosclerosis of the aorta or in the peripheral arteries

Incidence

Anatomic investigations on otherwise healthy soldiers in wartime have shown that at the ages of 18 to 20 coronary sclerosis is found in 40 per cent of the necropsies The average age of American soldiers killed in action in Korea was 22 2 years and the incidence of sclerosis was 77 3 per cent (Enos et al) In necropsies on 65 young soldiers during World War I atherosclerosis of the aorta and coronary arteries was 44 6 per cent of all cases In another series of 75 additional cases the same observer found atherosclerotic changes in 57 3 per cent (Monckeberg) The descending branch of the left coronary artery was most often affected

In 1000 consecutive autopsies Allan found coronary lesions in 371 the youngest patient affected was 13 years old In over 50 per cent of these cases a myocardial fibrosis had resulted from the coronary lesion From another study (Clawson) of 928 cases of coronary sclerosis it was concluded that this affection accounts for 25 per cent of all deaths from heart disease (exclusive of congenital heart lesions) and of 4 per cent of all deaths in individuals over 6 months old While myocarditis and diphtheritic involvement are the most common affections of the heart muscle in youthful patients coronary sclerosis with its resultant myocardial fibrosis is by far the most frequent affection in older individuals

According to Pyle and Russell the mortality from coronary sclerosis is highest among physicians and lowest among gardeners agricultural laborers and workers in chemical processes Others found no greater incidence among physicians than in the general population but a higher rate has been claimed among men engaged in sedentary occupations Morris found a lower incidence of coronary sclerosis in physically active people However in miners aged 55 to 64 the incidence of coronary sclerosis was 38 per cent (Thomas et al)

At the age of 35 and over a twofold to threefold increase has occurred in England and Wales in the death rates attributed to coronary disease in the last 15 years (Martin)

Further details will be discussed in the chapter on angina pectoris

Symptoms

Sometimes the lesion is betrayed by the symptoms of angina pectoris This occurs when the atherosclerotic process has led to the stenosis of a coronary artery the occlusion of the involved artery leads to the syndrome of myocardial infarction Very often however pain is absent even when a large branch of a coronary artery is completely blocked While reliable statistics are not available pain is mentioned in the history of only a minority of cases with fully developed coronary sclerosis

In many patients the lesion is asymptomatic Some consult the physician for vague complaints like fatigue or loss of appetite Some have gastrointestinal symptoms such as persistent meteorism eructations alternating diarrhea and constipation Since these symptoms are often pronounced in patients whose

circulation is fully compensated co existing sclerosis of the mesenteric vessels may be suspected if the action of reflexes and colonic spasm can be excluded

In many patients who consult their physicians for complaints relating to *hypertension* or *diabetes* evidence of coronary disease is discovered accidentally

In most cases the lesion remains unrecognized and unknown to the patient until some complication like coronary thrombosis or heart failure appears

Signs

Very few signs may be called pathognomonic for coronary sclerosis the most reliable is the discovery of a sclerotic coronary artery in an x ray film This finding however offers little diagnostic help because medial sclerosis without obstructive atherosclerosis may show deposits of lime salts

From a factual standpoint the diagnosis of coronary sclerosis one of the most prevalent cardiac lesions is made only by inference If a patient complains of anginal pain we may infer the existence of a coronary sclerosis on the basis of known facts If a patient over 40 years of age has evidence of heart failure or of cardiac dilatation with changes in the electrocardiogram indicative of myocardial involvement and there is no other cause (myocarditis uncomplicated hyper tension avitaminosis or infection) one may assume that coronary sclerosis exists This assumption is supported by the discovery of atherosclerosis in other arteries such as those of the fundus retinae

The diagnostic difficulties are exemplified by a study of 86 cases which came to necropsy with such diseases as carcinoma gastric ulcer and cirrhosis of the *liver and which showed marked coronary sclerosis (Willius and Brown)* The ages of the group varied from 33 to 81 years Seventy eight per cent were males Only 24 per cent had anginal pain In 40 per cent of the patients there was no subjective or objective evidence of cardiac disease

Accordingly at necropsy one is often surprised by the severity of the alter ations in the coronary arteries and even by those in the myocardium when the asymptomatic patient has presented no evidence of cardiac disease on clinical examination Physicians who appraise the hearts of elderly individuals prior to operation accept a great responsibility and should always bear in mind our limitations of knowledge It is better to state that the examination does not disclose coronary sclerosis than to say that coronary sclerosis is absent

Often the first sign of atherosclerosis is a harsh systolic murmur over the apical area or over the aorta At first this murmur may be audible only after exertion but later it is permanent In all probability this murmur depends upon sclerotic changes in the aortic valve so that it is not a direct sign of coronary sclerosis Nevertheless it is significant as indicative of an atherosclerotic process and is important when found in relatively young individuals In 86 consecutive necropsies in which coronary sclerosis was found ot per cent (44 cases) had sclerosis of the mitral or aortic valves In 17 per cent both valves were involved The remaining physical findings are similar to those elicited in other myocardial lesions and will be discussed in a later section

The electrocardiogram has been a great diagnostic aid and accounts for most correct diagnoses Nevertheless a normal electrocardiogram does not preclude the presence of advanced coronary sclerosis The electrocardiogram may remain normal when the lumen of the vessel is not markedly narrowed and therefore no myocardial ischemia develops The same thing happens when the lesions are small or when they are located in areas not clearly represented in the electrocardiogram One should also remember that profound changes in the electrocardiogram may vanish rapidly with the development of scar tissue and the progress of healing

At present coronary sclerosis is diagnosed much more frequently than in former years Whether or not this is due to an actual increased incidence is not fully decided While pathologists report an increase it is equally true that they inspect the coronary arteries more carefully than in the past The refinement of methods of examination and the fact that the term coronary sclerosis is generally used when formerly a diagnosis of dropsy cardiac insufficiency angina pectoris and the like would have been made are certainly responsible for the apparent increased incidence of the lesion

Therapy

There is no specific therapy for coronary sclerosis

All types of fat should be restricted Plant sterols are not absorbed from the human gastrointestinal tract in appreciable amounts However they must be restricted as well since cholesterol values in the serum rise when vegetable fat is added to the diet of patients on cholesterol poor food

The ingestion of neutral fat should also be restricted since fat facilitates the absorption of cholesterol A reduction in the caloric intake in general seems to be important (see later) The rice diet and similar fat free diets have shown that it is possible to diminish the cholesterol content of the serum by 20 to 40 per cent

The so called lipotropic substances such as inositol choline and methionine seem to be without value Serum cholesterol levels are said to be lowered by polysorbate 80 choline inositol complexes This agent increases the stability of lipid emulsions

Estrogens seem to clear the plasma from high molecular lipids (Pick et al) They increase the phospholipids in cockerels lower the cholesterol phospholipids ratio and atherosclerotic plaques are perhaps reabsorbed We recommend continuous administration of estrogens to all postmenopausal women with hypertension diabetes or a family history of coronary artery disease In man unfortunately this therapy leads to unpleasant side effects

Estrogens have to be given in large amounts in order to be effective in changing the abnormal lipid pattern of the blood to a normal one This problem is under study at the present time

Soybean sterols mainly sitosterol admixed to the diet has been said to lower plasma cholesterol markedly It may interfere with the absorption of cholesterol

(Peterson) Eight grams of sitosterol are given before meals (Best et al) However Wilkinson et al working with ambulatory patients were unable to achieve sustained reductions in the level of the blood cholesterol The substance needs further evaluation

Cytellin a mixture of beta sitosterols with dihydrobeta sitosterols is available One gives 8 to 10 grams 2 to 3 tablespoons per day orally in the form of a suspension

Patients with hypercholesteremia may develop thromboembolic phenomena when they are under therapy with corticotropin or cortisone (Adlersberg et al) In patients with hypercholesterolemia large doses of nicotinic acid cause the blood lipid pattern to change toward normal (Altschul et al) Three to 6 grams of nicotinic acid are given daily Side reactions such as flushing and pruritus diminish rapidly after a few days of treatment Urticaria and vomiting disappear within a few days after discontinuation of the treatment and do not reappear when treatment is resumed

Essential unsaturated fatty acids particularly linoleic acid are now recommended in capsule form in order to lower the cholesterol level of the blood Nicotinic acid and pyridoxin are added

In addition to diet hormonal hereditary and other factors play a role but a fat poor diet is the strongest weapon available at present against atherosclerosis

The chylomicrons which appear in the blood following the absorption of fat disappear following the intravenous injection of heparin (Hahn) but the use of heparin injections (daily or twice weekly) as recommended did not yield convincing results in patients with evidence of coronary sclerosis It has been claimed that this therapy improves angina on effort and similar complaints rapidly Whether it prevents the progression or development of atherosclerosis is not established

MYOPATHIES

There is a small group of cases in which clinical and pathologic examination including histologic sections fail to reveal the diagnosis and the nature of the myocardial lesion The heart is enlarged and evidence of heart failure is observed prior to death but the coronary arteries are normal and patent No previous hypertension existed histologically the myocardium seems normal The expression myopathy has been coined for these cases Clinicians occasionally use the term myocardosis Wuhrmann defines myocardosis as a change in the myocardium without cellular interstitial infiltrations there is evidence of fatty degeneration and cloudy swelling These cellular degenerations are encountered in Laennec s cirrhosis in hepatitis in the nephrotic syndrome in alcoholism and sepsis and are explained by a dysproteinemia If the cells die myocardial fibrosis may follow

Undoubtedly many patients placed in this category belong to the group of nutritional disturbances (e g thiamine deficiency) While microscopic changes

are demonstrable in advanced stages of the lesion in all probability there are periods in which the rather crude histologic methods now available fail to reveal an alteration of the myocardial fibers

It is precisely in myocardial disease that the unreliability of anatomic and histologic methods of examination impresses one most distinctly A normal microscopic appearance does not show whether the heart functioned normally and efficiently It has been pointed out that it is often impossible to explain heart weakness and cardiac death anatomically Often the pathologist cannot tell why a patient who responded excellently to digitalis for years suddenly ceased to react to treatment When asked whether the heart muscle was sufficiently strong to compensate for a valvular lesion the pathologist can answer only by examining the liver lungs or kidneys the heart itself reveals nothing

This experience was responsible for the chemical study of the heart muscle with the hope of finding significant changes which were not disclosed by histologic methods Changes were anticipated since creatine potassium and phosphorus play a definite role in muscular contraction The amounts of phosphatides of calcium of creatine and of potassium in the hearts of patients with an abnormal or weak myocardium were found to be altered

Abnormalities of this kind may lead to cardiac failure but the evaluation of these findings and the application to the clinic is still remote

INVOLVEMENT OF THE MYOCARDIUM IN OTHER DISEASES

Tumors The heart muscle is frequently invaded by tumors from neighboring organs and in rare cases is the site of primary growths these are discussed briefly in connection with pericardial new growths

Sarcoidosis Death from cardiac failure is not unusual in sarcoidosis (Boeck s sarcoid Schaumann s disease) While a detailed description of this disease is beyond the scope of the present book attention may be directed to a few clinical features all of which although common are rarely present in a single case

The superficial lymph nodes are often enlarged and the skin may show a variety of lesions (lupus pernio of Besnier) The pulmonary infiltrations and enlargement of the mediastinal lymph nodes closely simulate the involvement of tuberculosis Focal destruction of bone occurs in the distal parts of the extremities Iridocyclitis is often combined with enlargement of the parotid gland and fever The red blood cells are hypochromic the sedimentation rate is increased and occasionally an eosinophilia or monocytosis dominates the blood picture If superficial glands are involved biopsy of the firm grey noncaseating nodules which may reach 1 cm in diameter will disclose tubercle like granulomas composed of epithelioid and giant cells of a foreign body type

The etiology of this disease is unknown nonspecific allergy is suspected to exist but has not been proved Many arguments speak in favor of a tuberculous origin While it affects the white and black races the vast majority of American cases have been in Negroes The course has an insidious onset and is characterized

by a slow advance that may be punctuated by remissions or recovery Bundle branch block and atrioventricular block are common Death occurs usually from heart failure although cardiac clinical manifestations stand in the background until the disease is far advanced

Sickle Cell Disease Another disease associated with cardiac hypertrophy and chronic cardiac failure is sickle cell anemia If as often happens the patient has recurrent attacks of painful joints and a systolic murmur at the apex as well as an enlarged right ventricle involving mainly the outflow tract the erroneous diagnosis of rheumatic heart disease is frequently made Anginal retrosternal pain is not rare Occasionally epistaxis is seen The left atrium may be enlarged but rarely to a marked degree The P R interval may be prolonged The RS T segment is often depressed and the T waves are abnormal This chronic hereditary familial disease is confined almost exclusively to Negroes Apart from the sickle cell trait a rather common intrinsic defect of the erythrocyte in Negroes an anemia is often present with the red cell count down to 1 000 000 cells Highly characteristic are the punched out ulcers near the ankles which simulate the ulcerations of syphilis Activity of the disease is often reflected in attacks of abdominal pain nausea vomiting and moderate jaundice which may closely mimic an acute abdominal emergency Sometimes the bone changes which consist of peculiar radial striations are highly suggestive

A variety of neurologic manifestations due to thrombosis of different vessels supplying the central nervous system dominates the clinical picture in other cases The combination of anemia thrombosis and jaundice together with the cardiac findings previously mentioned may suggest a subacute bacterial endocarditis although confusion with a rheumatic carditis is more common The cardiac changes are due partly to the occlusion by sickle cells of small vessels in the lesser circuit and partly to a similar process in the coronary arteries The anemia also plays a role

For differential diagnosis from rheumatic fever which may be difficult one should consider the normal sedimentation rate the normal left atrium and the absence of relief from salicylates in sickling disease In this condition the pain is also located more over the bones than over the joints On rare occasions rheumatic heart disease and sickling were seen simultaneously in the same patient

Von Gierke's Disease Another disease characterized frequently by cardiac enlargement and symptoms of heart failure in a child is Von Gierke's disease or glycogen storage disease In the more common hepatic type the liver is greatly enlarged the fasting blood sugar level is low sensitivity to insulin is increased and the elevation of blood sugar following the injection of epinephrine is smaller than normal Ketonuria without glycosuria is often in evidence In the cardiac type enlargement of the liver and kidneys may be slight and the fasting hypoglycemia and ketonuria are usually absent Both varieties may be associated with mental retardation and epileptiform seizures The outlook in the cardiac type is very unfavorable and treatment of the heart failure by the usual remedies is unsatisfactory

Idiopathic cardiac hypertrophy that is hypertrophy of the heart without any visible cause comprises a variety of conditions Formerly patients with thiamine deficiency or primary pulmonary hypertension were included and the condition is more rarely diagnosed with advance of our knowledge

The abnormality is found more often in males Increased deposits of glycogen were found in familial types (Evans) In many patients with this syndrome increased fibrosis is found at post mortem so that one of the myocardial diseases of unknown etiology mentioned above have to be assumed In such cases the term idiopathic hypertrophy is not really correct

There are numerous other diseases with cardiac repercussions but in general the alterations of the heart are interesting incidental findings rather than essential features of the process

SYMPTOMS AND SIGNS OF THE MYOCARDIAL DISEASES

Many symptoms and signs specific for myocardial lesions have been mentioned in previous chapters and some of the clinical features of cardiac involvement in tonsillitis diphtheria thiamine deficiency and coronary sclerosis have been reviewed In the present section the chief symptoms and signs common to all myocardial affections will be discussed

Dyspnea If heart failure supervenes dyspnea particularly nocturnal dyspnea occurs in all myocardial lesions for in all of them including coronary sclerosis the left ventricle is predominantly damaged This group includes the great bulk of patients whose nights are made sleepless by Cheyne Stokes respiration Such patients are often treated for asthma with epinephrine and asthma remedies so that a considerable period may elapse before the cardiac disease is recognized

Pulse The peripheral arterial pulse may be rather small if the myocardium is badly damaged It is understandable that the diminution of contractile power of the left ventricle will reduce the stroke volume whenever the myocardium is profoundly injured Naturally a small pulse since it is present only when myocardial failure is advanced is a very unfavorable prognostic sign

Palpation The results of palpation over the cardiac area are meager The left ventricle is chiefly involved and its pulsations are often not felt normally Many patients are advanced in age with the result that the heart is covered by emphysematous lungs Finally a heart with a damaged myocardium reveals weaker pulsations than one with a healthy muscle In some cases however the presence of a heaving apex beat indicates marked hypertrophy of the left ventricle In other patients with pulmonary congestion the closure of the pulmonic valves is palpable If gallop rhythm is present it can often be detected by palpating the chest between the lower end of the sternum and the apical area (see below)

Percussion As pointed out earlier percussion often reveals a heart of normal size despite considerable myocardial damage Later percussion shows (as x ray confirms) an aortic configuration Finally with the development of back pressure in the lesser circuit mitralization appear In this stage even dilatation of the left atrium may be found when the patient is examined in the right oblique

position with the administration of barium to visualize the esophagus If the heart is strikingly large in myocardial disease (cor bovinum) without relative mitral or tricuspid insufficiency being present the existence of hypertension should be suspected even if the blood pressure is normal at the time of examination

The size and shape of the heart in late stages with dilatation to the right and left as well as mitralization closely resemble the picture presented by combined mitral aortic stenosis and tricuspid lesions or the one occasionally seen in pericardial effusions The absence of pulsations along the cardiac border on fluoroscopy in cases with severe myocardial damage strongly suggests the latter

Auscultation Not rarely auscultation yields normal findings Normal pure and loud heart sounds may be heard despite a very advanced myocardial lesion This is the chief reason why the examiner is led astray in those cases in which percussion has not provided satisfactory results Sinus tachycardia is common but bradycardia may also be present

Often soft or distant heart sounds are considered evidence of myocardial disease As a matter of fact the heart sounds may become more distant as the disease progresses and louder with recovery from myocardial damage Usually however there has been no opportunity to examine the patient earlier for comparison so that the discovery of distant heart sounds cannot be unequivocally attributed to myocardial damage Even slight superimposition of the lung over the heart in the precordial area or obesity may make the heart sounds distant Heart sounds are also distant in patients with a markedly convex thorax and a deep position of the heart

Abnormal accentuation of the heart sounds splitting of the first or second heart sound are common findings but they must be interpreted with great care as evidence of myocardial disease such signs may be elicited in young healthy individuals as well as in cases of cardiac neuroses and hyperthyroidism

Often no systolic apical or aortic murmurs are audible When present they should always be regarded with suspicion and must be distinguished from physiologic innocent murmurs Every systolic murmur — those of recent appearance in particular — demands careful examination

When for any reason the left ventricle undergoes a marked dilatation relative mitral insufficiency may appear If the patient is seen when the lesions are fully developed it is often difficult to decide whether he has a relative mitral incompetence or a structural one of rheumatic origin

Not uncommonly great dilatation of the right ventricle causes relative tricuspid insufficiency

Electrocardiogram The electrocardiogram has paramount importance in the diagnosis of myocardial lesions Slurring notching or widening of the QRS complexes abnormalities of the RS T segments and T waves in leads I and II and the chest leads are of great significance In acute isolated myocarditis an elevated PS T segment (as in acute myocardial infarction) has been observed (Gillis and Walters) probably due to patchy necrosis of superficial myocardial fibers

It must be pointed out again that a normal electrocardiogram does not preclude the presence of a severe myocardial lesion moreover repeated tracings must be obtained for the alterations are often transient Therefore in diseases known to have a high incidence of myocardial involvement such as rheumatic fever the electrocardiogram should be recorded frequently but in chronic diseases the interval between tracings may be as long as six months provided the symptoms and signs remain unchanged

Practical experience shows unfortunately that insufficient knowledge of the normal variations of the electrocardiogram very often leads to an unjustified diagnosis of a myocardial lesion Therefore great caution must be observed before a heart muscle is pronounced abnormal on the basis of the electrocardiogram alone

Gallop Rhythm

Gallop rhythm is an extremely important auscultatory sign in myocardial disease It is however ambiguous and should be evaluated only in conjunction with other clinical signs

The first and sometimes difficult task is the distinction between splitting (duplication) of the heart sounds and gallop rhythm This differentiation is usually based on the fact that in gallop rhythm the third sound is separated from the other sounds by an appreciable interval whereas the interval between the two parts of a split sound is extremely brief Thus in cases without prolongation of atrioventricular conduction time the sound caused by the atrial contraction appears very shortly before the first heart sound In some cases however recourse to graphic registration of the heart sounds is necessary in order to differentiate between these phenomena

If less important details and minor differential points are disregarded four types of gallop rhythm should be differentiated (1) Protodiastolic gallop rhythm (2) Presystolic gallop rhythm (3) Summation gallop rhythm (4) Systolic gallop rhythm

(1) PROTODIASTOLIC GALLOP RHYTHM This originates in a mechanism similar to that of the physiologic heart sound and creates a similar impression on the examiner (figure 45) The third heart sound is a very common finding in children and healthy young adults but it disappears in the adult With development of myocardial damage the rush of blood into the atonic left ventricle may cause the third heart sound to appear early in diastole even in adults This is the protodiastolic gallop rhythm The new sound is explained by vibrations of the ventricular wall or the valves (Lewis and Dock) when the ventricle fills the sound is prone to occur when this filling takes place under increased pressure caused by congestion According to other observers protodiastolic gallop rhythm is caused by the impact of the left ventricle on surrounding structures during diastolic filling

Differentiation from a normal third heart sound is impossible by auscultation or graphic registration If an organic heart lesion is present the new sound is presumed to be due to gallop rhythm Some think the differentiation can be accomplished by the following means (Bramwell) the third heart sound cannot be

palpated it is closer to the second sound than is the new sound in gallop and the third heart sound can be heard with a normal rate whereas gallop rhythm is observed usually with increased rates There are cases however particularly in the younger age group in which differentiation is impossible If the patient is over 30 years old a gallop rhythm can usually be safely assumed for a physiologic third heart sound is rare at this age

(2) PRESYSTOLIC GALLOP RHYTHM In this type the new heart sound precedes the two normal heart sounds by an interval which is usually longer than that in a split first sound (figure 45)

It happens however that occasionally this interval is not sufficiently prolonged to permit differentiation without recourse to graphic methods Heart sound registration shows that the new sound is definitely presystolic whereas in mere splitting of the first heart sound it is systolic

The mechanism responsible for this type of gallop rhythm is disputed While many still believe that an audible contraction of the atria is responsible there are strong arguments to support the assumption that its mechanism is similar to that causing *protodiastolic gallop rhythm Considered in this light* the cause would be again found in ventricular filling as affected by atrial systole Thus both types of gallop rhythm would have the same origin If the P R interval is prolonged the atrial contraction occurs earlier in diastole gallop rhythm is then common for a summation takes place (see below)

(3) SUMMATION GALLOP RHYTHM This is the most common form It is heard when the heart rate is accelerated (usually over 100 beats per minute) or with a prolonged P R interval Under these conditions vibrations due to early filling of the ventricle coincide with vibrations created by systole of the atrium and *gallop rhythm appears Thus many times when each factor alone does not suffice* to cause gallop rhythm the combination produces a distinct new heart sound It is clear from this definition that even the physiologic third heart sound often will become intensified or audible with an acceleration of rate owing to this summation factor

This mechanism of summation also makes understandable the findings of those investigators who concluded that protodiastolic gallop rhythm is bound to atrial contraction In the patients examined by them a summation gallop existed

The importance of rate for the appearance of gallop rhythm is easily demonstrated Often a gallop rhythm disappears when a fast rate is slowed by treatment or even temporarily slowed by carotid pressure

(4) SYSTOLIC GALLOP RHYTHM (SYSTOLIC CLICK) This form was described a long time ago by Potain Two types are differentiated The mechanism of one heard best over the apex is unknown The other and more common type is heard at the base of the heart and derives from changes of the tonus of the aorta and pulmonary artery under the systolic impact of blood It has been found in typhoid fever tuberculosis and in nervous individuals It does not seem to be a significant *sign of cardiac disease* but is often confused with diastolic gallop

rhythm Rarely pericardial or pleuropericardial adhesions may cause a similar phenomenon

Frequency In 1353 consecutive cardiac patients gallop rhythm was found in 62 (Bramwell) In 50 of these the heart rate varied between 90 and 120 In 60

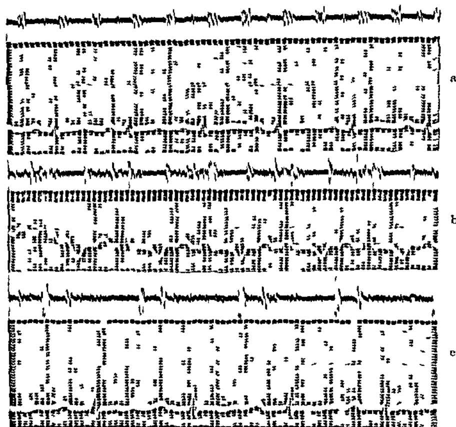


FIG 45 Three instances of gallop rhythm The top tracing (a) shows a gallop rhythm in a patient with coronary sclerosis and myocardial failure The three heart sounds are clearly visible There is a sinus tachycardia a summation gallop developed The middle tracing (b) also shows a summation gallop in a patient with hypertension and marked hypertrophy and dilatation of the left ventricle In the lowermost tracing (c) the P R interval in a patient with coronary sclerosis was prolonged to 0 24 second The first heart sound was dull and shows low vibrations in the stethogram while the second heart sound was accentuated This is an instance of presystolic gallop

cases of gallop rhythm (Wolferth and Margolies) the protodiastolic type was present 14 times the presystolic type 2_ times and a summation gallop 24 times

Clinical Aspects The new sound in gallop rhythm is dull and of low pitch It is heard best over the apex the lower sternum and at a point between these two areas Often it is present only when the patient stands or after light exertion due

to the increase of rate In most patients it is heard better in the supine position It has often been stated especially by the French school that gallop rhythm over the lower sternum develops in the right ventricle whereas the type heard best over the apex originates in the left ventricle While some authorities accept this differentiation it is our experience that very commonly gallop rhythm is detected only over the lower sternum in cases of coronary sclerosis or hypertension in the absence of hepatic or venous engorgement that is in cases of left ventricular damage

Gallop rhythm is frequently palpable The rapid succession of heart sounds creates three impacts resulting in the appearance of a peculiar and characteristic sensation which older workers called tremor cordis

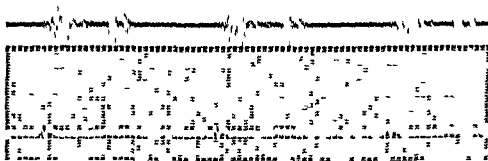


FIG 46 Split second sound in a patient with left bundle branch block (Lead II)

With the appearance of atrial fibrillation and the cessation of effective atrial contractions gallop rhythm often disappears But the assertion that gallop rhythm does not occur during atrial fibrillation is certainly incorrect That type of gallop rhythm which is produced by the flow of blood into the ventricles during the early part of diastole may persist despite fibrillation Only the presystolic and summation types vanish

Differential Diagnosis Mitral stenosis is sometimes difficult to exclude The diastolic apical murmur of mitral stenosis is brief low pitched and mid diastolic often it closely resembles a third heart sound An enlarged left atrium may be present because of left ventricular failure

In cases of continuous bigeminal rhythm caused by extrasystoles occasionally the first sound of the extrasystole alone is heard while the second sound is absent This happens particularly when the extrasystoles are very premature and filling of the ventricle is insufficient systole is then so weak that the semilunar valves are not even opened and no second sound appears In these cases three loud sounds are heard which may cause confusion with gallop rhythm

Clinical Importance Very often gallop rhythm heralds the beginning of myocardial weakness long before other evidence appears It is notably common in cases of myocardial damage and hypertension with an increased heart rate It is however not rare in patients with a normal pressure and a normal or slow rate

Under certain conditions it has no great importance Thus in rheumatic fever the sinus tachycardia and the prolongation of the P R interval may lead to a summation gallop rhythm which does not necessarily indicate myocardial weakness In most cases however gallop rhythm is the 'cry of the heart for help' and suggests the administration of digitalis It is an ominous sign with an acute coronary thrombosis and its importance here is obvious from the fact that among 62 cases observed by Bramwell only 15 survived for more than 18 months

Gallop rhythm is commonly encountered in patients with intraventricular block (bundle branch block arborization block) (White) This finding is apparently coincidental however since gallop rhythm and intraventricular block are both due to myocardial damage Splitting of the second heart sound is common in bundle branch block (figure 46)

Gallop rhythm is rarely discovered by those physicians whose attention has not been specifically drawn to this phenomenon at the time of under or post graduate instruction This finding is more important than the discovery of a murmur Therefore it is important that those charged with the responsibility of instructing medical students make sure that every student becomes familiar with gallop rhythm

Pulsus Alternans

Pulsus alternans is another valuable sign of myocardial weakness and myocardial disease By this term one understands the regular alternation of large and small pulses with rhythmic cardiac actions Accordingly this phenomenon is absent in atrial fibrillation Very often it is absent during regular sinus rhythm but immediately follows extrasystoles for a long or short series of beats (figure 95)

Incidence Among the radial pulse tracings of 300 cardiac and cardiovascular patients pulsus alternans was found in 71 (White) The phenomenon appeared temporarily only after extrasystoles in 55

Diagnosis In outspoken cases it is detected at once by ordinary palpation of the radial artery Every second pulse is smaller In a few cases we have been able to count only half as many pulses in a peripheral artery as heart beats heard by auscultation Thus a patient with 96 rhythmic beats per minute may have *a pulse rate of only 48 When pulsus alternans is not immediately obvious by* simple palpation it can often be elicited by slight compression of the brachial artery with one hand and simultaneous palpation of the radial pulse in the same arm with the other

Figure 47 shows a pulsus alternans in a pulse tracing (sphygmogram) The simplest method however for discovering a slight pulsus alternans is sphygmomanometry since the stronger beats also provide higher pressure Thus one may find that between the pressure of 150 and 160 mm Hg or between 140 and 160 only alternate beats are transmitted below the cuff (discovered by palpation or auscultation) The height of the diastolic blood pressure also alternates

The phenomenon is often overlooked since in determining the blood pressure the examiner usually does not bother to ascertain whether every beat or every

other beat reaches the periphery just below the upper limit of the systolic blood pressure If however one searches regularly for this phenomenon while taking blood pressure the incidence of pulsus alternans is surprisingly high particularly in a decompensated nondigitalized patient with hypertension Although not uncommon with a normal blood pressure it is then a little more unfavorable from a prognostic standpoint An alternating pulse was found in 33 per cent of decompensated patients

Occasionally the loudness of the second aortic sound or of a systolic murmur likewise varies in intensity with the alternating beats In rare instances alternating cardiac action can be observed fluoroscopically in the form of alternating strong and weak contractions These alternations were recorded by roentgen kymograph (Scherf and Zdansky)



Fig 47 Pulsus alternans

Alternation of waves of the electrocardiogram is usually independent from an alternation of the pulse and is due to abnormal (alternating) spread of the excitation wave over the heart (electric alternans)

To differentiate an alternating pulse from a bigeminal pulse it is important to note that in extrasystoles the smaller pulse wave is usually premature whereas in pulsus alternans it is slightly delayed

The pulsus alternans has been found to disappear or to be greatly diminished when the patient develops congestive heart failure (Ryan et al) This may be connected with the increase of the ventricular diastolic filling pressure in failure

Mechanism Since the original description by Traube and Gaskell many attempts have been made to explain this interesting phenomenon which is easily produced in the experimental animal by poisoning the heart with a great variety of substances

A difference in the excitability of myocardial fibers is generally assumed to be causal The conception of De Boer is at present widely accepted If V represents the whole myocardium and V_1 and V_2 a smaller and larger part of some what damaged myocardial fibers one may assume that in pulsus alternans the heart contracts according to the formula $V - V_1$ $V - V_2$ $V - V_1$ and so forth In other words with one systole a small part of the myocardium does not participate with the next beat a larger part does not contract Certain observations lead to the assumption that the whole ventricular muscle never contracts

The opinion that pulsus alternans is primarily due to a change of cardiac filling (Wenckebach) has not been completely discarded however an alternans

can be observed in an empty heart or in a muscle strip indicating that the essential factor is probably in the muscle

Significance In a large majority of cases the phenomenon is of serious importance because of its indication of myocardial damage Often it disappears with digitalization Patients presenting it rarely survive for more than a few years after its discovery (Windle) In one patient a distinct pulsus alternans was observed by one of us for seven years that is for two years after the paper by the author (Swildens) was concluded

Pulsus alternans is found in otherwise healthy individuals during an attack of paroxysmal tachycardia with very high ventricular rate Under these circumstances the phenomenon is without significance and vanishes with the disappearance of the tachycardia

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Chapter 14

Diseases of the Pericardium

ISOLATED DISEASE of the pericardium is uncommon but secondary involvement the result of extension of a process from some neighboring organ infection from the blood stream or participation in systemic diseases occurs in a host of di orders Frequently the local pericardial manifestations are submerged in the general symptoms of the primary disease but sometimes they dominate the clinical picture

ANATOMY AND PHYSIOLOGY

The parietal pericardium resembles an asymmetric cone whose apex extends to the aortic arch and whose base is the diaphragm The anterior surface of the pericardium looks somewhat like a right angled triangle since the right side descends almost perpendicularly and the diaphragmatic attachment is more or less horizontal Pleura covers most of the sternocostal surface of the pericardium with the exception of a small uncovered area to the left of the lower sternum Through this triangle of safety pericardiocentesis can be performed without entering the pleura The internal mammary artery is situated 2 5 cm from the left sternal border It escapes injury if paracentesis is performed in the uncovered area at least 3—4 cm to the left of the left sternal border

The parietal pericardium possesses an inner serous and a middle fibrous layer as well as the pericardial connective tissue which unites it to adjacent organs The visceral pericardium is approximately 5—10 microns thick

Since the heart does not entirely fill the pericardial cavity potential spaces exist Normally the cavity contains about 25 ml of viscid fluid whose physio chemical properties approximate those of fluids in other serous lined cavities When a pericardial effusion forms the parietal membrane unfolds and about 150—250 ml the average capacity of the normal adult pericardial cavity can collect in the various pericardial recesses before much pressure is exerted At least this much volume must accumulate before an effusion can be detected by physical examination According to others the diagnosis is often missed if less than 500 ml of fluid are present (Camp and White)

Undue cardiac movements are prevented by the pericardium and its attach ments to nearby structures and to the thoracic cage Alterations of these attach ments may change the configuration of the heart thus descent of the diaphragm pulls on its pericardial attachment and the heart drops when the diaphragm is

elevated by pregnancy or obesity the heart becomes transverse The significance of the suspensory function of the pericardium becomes more apparent when external pericardial adhesions angulate or rotate the heart and produce clinical manifestations

The pericardium also seems to exert a protective influence The relative rigidity of the fibrous layer is considered an important factor in preventing excessive dilatation of the heart during emergencies The pericardium is not elastic Moreover the pericardium may offer some protection against cardiac infection for at times inflammations may involve the outer aspect of the pericardium without penetrating the cavity Pyopericardium is particularly common in patients with pneumonias of the lower lobe of the left lung this has been accounted for by the relative thinness of the membrane over the left ventricle

The pericardial serosa is admirably designed to minimize friction during cardiac contractions If the pericardium is removed surgically the pleura changes and adapts itself to this function

Although pericardial diseases are often listed among the painful disorders and special nerve endings can be demonstrated in the membrane clinical experience teaches that most forms of pericarditis are painless experimental studies also indicate that the membrane is rather insensitive Generally speaking the occurrence of pain in a pericardial disease indicates an involvement of some adjacent structure Thus pain in the precordial area aggravated by inspiration and pressure is often due to associated anterior mediastinitis Sharp as well as dull pain in the same area is often noted in an acute myocarditis which regularly accompanies acute pericarditis Neck pain is felt when a pleuropericarditis extends to the area of the diaphragm innervated by the phrenic nerve Dorsal pain is often present if the inflammation involves the tissues of the posterior mediastinum (Capps and Coleman) The pericardium is also relatively insensitive to nonpainful stimuli such as touch rubbing moderate heat cold and so forth

FIBRINOUS PERICARDITIS

Introduction

Pericarditis is the most common disorder of the pericardium it was present in 3 7 per cent of 36 743 necropsies compiled by the authors Possibly this is an underestimation of its incidence since routine microscopic search has not been conducted by many pathologists

Pericardial inflammation can be classified in a number of ways for example according to the etiology or pathology However a discussion of each would entail considerable repetition Thus streptococci may excite a fibrinous serous hemorrhagic or purulent pericarditis Pyopericardium may be produced by streptococci staphylococci pneumococci etc For these reasons and in the interest of brevity it has seemed advisable to select certain general forms of pericarditis for discussion and to amplify these remarks briefly in connection with some important clinical entities

Acute fibrinous pericarditis pericarditis sicca dry pericarditis may be regarded as the mildest form of pericardial inflammation For cases in which serous fluid collects the term serofibrinous pericarditis is appropriate

Etiology

An enumeration of all possible causes is pointless since any agent capable of irritating the pericardium may be responsible Moreover most of the provocative factors can evoke other forms of pericarditis if the stimulus is more intense

In a vast majority of instances an infection is responsible The coccal infections — pneumo meningo staphylo and gonococcal — are most common Bacillary infection is exemplified by tuberculosis leprosy and more rarely by the typhoid colon group of organisms Higher forms such as actinomyces and even animal parasites (amoeba trichinella and filaria) may also invade the pericardial cavity Pericarditis occurs in trypanosome infection (Rosenbaum et al)

Fibrinous pericarditis is relatively infrequent in subacute bacterial endocarditis in fact the presence of a friction rub has been used as a differential sign between rheumatic carditis and subacute bacterial endocarditis It should be emphasized however that both of the latter conditions often coexist

In many of the exanthemata secondary infection causes pericarditis In some other diseases bacillary dysentery and Asiatic cholera for example dryness of the serosa rather than infection seems responsible for the friction rub since there is no true pericarditis For unknown reasons syphilis of the pericardium is exceedingly uncommon

Several other varieties of fibrinous pericarditis will be discussed elsewhere in this book Traumatic pericarditis is discussed in the chapter on cardiac trauma infarction pericarditis pericarditis over cardiac aneurysms the pericarditis in lupus erythematosus and pericarditis in periarteritis nodosa are discussed in the respective chapters Some of these varieties as well as the pericarditis sometimes seen in Boeck s sarcoid often escape clinical detection

Pericarditis may be excited by some chemical agents In this group belong uremic pericarditis and perhaps pericarditis following coronary occlusion with myocardial infarction The intrapericardial injection of many drugs causes inflammation and has even led to fatal constrictive pericarditis (Beck)

Pericarditis may be induced by physical agents The introduction of small particles of talcum (Thompson and Raisbeck) bone silica and the like into the pericardial cavity causes fibrinous inflammation and the formation of adhesions Likewise foreign bodies (bullets) in the pericardial cavity have occasionally been responsible Neoplasms invading the pericardium may also excite pericarditis Sometimes substances are intentionally placed in the cavity to excite inflammation in the hope that the newly formed blood vessels will provide an additional blood supply for the myocardium

Fibrinous pericarditis may follow roentgen therapy to the chest for hyperthyroidism or Hodgkin s disease and the implantation of radium for carcinoma

of the esophagus The acute mediastino cardiac reaction consists of precordial pain aggravated by movement of the chest fever no significant physical signs but electrocardiographic evidence of pericarditis

Acute pericarditis has been observed in serum sickness (Goldman and Low)

Terminal pericarditis apparently caused by a terminal infection is demonstrable only at necropsy It is neither a clinical nor pathologic entity It is common constituting about 10 per cent of all pericardial diseases Coincident but unrelated cardiovascular disease is present in about 50 per cent of the patients hypertensive cardiovascular disease providing the largest contingent Diabetes mellitus chronic nephritis and neoplasms may also be associated with terminal pericarditis Many other patients have an intrathoracic infection

Pathology

In fibrinous pericarditis the membrane loses its luster becomes rough and feels sandy If the amount of fibrin increases coagulated exudate forms small tufts whose appearance has given rise to many descriptive terms bread and butter heart cor villosum cor hirsutum and the like If the formation of fluid dominates it may contain floccules of fibrin while grossly the membranes show less striking changes Healing is followed by the absorption of exudate by the formation of milk spots or by adhesions between the epicardium and pericardium

The pathology elsewhere depends upon the primary disease In nearly half of the cases an intrathoracic infection (pneumonia empyema pulmonary abscess tuberculosis) will be found Most of the remainder will have some cardiovascular disease (rheumatic fever coronary thrombosis with myocardial infarction nephritis or nephrosclerosis with uremia) A small percentage has an extrathoracic infection or one of the wasting diseases mentioned as being present in terminal pericarditis

Symptoms

As implied above the clinical picture varies in accordance with the associated disease If pericarditis complicates some other infectious disease there may be little to suggest the new complication Sometimes the general symptoms become worse and the fever is somewhat higher or delirium appears in a previously lucid individual Usually however the onset is too insidious to be discerned In some patients with pericarditis the onset may be abrupt with chills fever and local pain

Pure fibrinous pericarditis is often a painless disorder and no distress is felt in uremic pericarditis or in the types associated with many chronic diseases If however neighboring structures are affected — the usual event in the common infectious diseases — there may be pain Thus two thirds of the cases presenting clinically demonstrable rheumatic fibrinous pericarditis and many instances of pericarditis associated with pulmonary infection present retrosternal precordial or left nipple pain This pain may be very intense

The local discomfort which is often described as oppression or tension may receive little attention if the patient is preoccupied with the more obvious general illness While the indefinite precordial sensations contribute to the anxiety they seem too vague for report by the patient In some patients the pain is sticking boring lancinating or constrictive but in others it is dull and heavy If intense it may be accentuated by changes of position local pressure breathing and coughing

Apart from these common variants the distress may be referred mainly to the abdomen and the syndrome may then simulate a ruptured viscus Operations for acute appendicitis have been mistakenly undertaken in children suffering from acute fibrinous pericarditis The dorsal pain is confused with a myositis the pain in the neck or diaphragmatic pain may be equally misleading

If respiration aggravates the distress superficial respiration with inadequate ventilation may cause cyanosis and dyspnea Cutaneous hyperesthesia may preclude percussion of the precordium

Signs

If the patient is placed in the proper position and can tolerate the pressure of the hand a fine or rough rub may be palpable This friction fremitus may be biphasic and may follow the apical impulse

The most important diagnostic sign a friction rub on auscultation is absent or eludes detection in over 75 per cent of the cases All gradations are encountered from a mild whisk to rough scraping The rub may be audible over the entire precordium Often it is heard only in a limited region over the area of absolute cardiac dullness for example it may appear only when the patient assume a definite position or in a single phase of respiration

Since the friction sound is provoked by cardiac movements it may be limited to systole or diastole but ordinarily it is heard in both phases When typical the rub is tripartite or appears in four phases (locomotive type) In these instances a rub is audible during diastolic inflow of blood and during systole of the atria as well as the ventricles

The distinction from endocardial murmurs is usually easy for the experienced physician but difficult for the beginner The friction sound tends to be circumscribed to lack a punctum maximum to be transient to change its location and time to lack a sharp association with systole or diastole to sound superficial to present an uniformly monotonous character without a crescendo or decrescendo phase to change during the respiratory cycle and in different positions and to be accentuated by local pressure or by extension of the head Pleuropericardial sounds are rare in the area of absolute cardiac dullness and often vanish during a certain phase of respiration

The friction rub heard over the apical area in patients with marked enlargement of the heart was mentioned on p 60 It is often associated with the large hearts of hypertensives and in children with an old rheumatic heart lesion when the heart approaches the inner surface of the left chest The friction rub limited

to the pulmonary conus in patients with hyperthyroidism is discussed in the appropiate section In all these conditions the friction rub is not due to pericarditis

In some cases of acute pericarditis the skin over the precordium may be edematous The temperature of the skin is often elevated (Elias)

X ray offers no assistance in the diagnosis of fibrinous pericarditis

Electrocardiogram

Knowledge of the electrocardiographic changes is important if confusion with coronary thrombosis is to be avoided The major change is in the RS T segment which is displaced upward or shows a high take off in all leads The QRS complex remains normal The RS T segment may show a curve with its concavity directed upward These changes usually last about one week At this time the RS T segment is found again in the base line and the T waves are bifid disappear or become inverted Ultimately the electrocardiogram reverts to normal provided no other cardiac disease is present

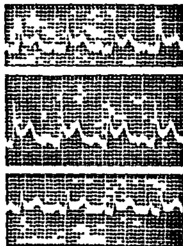


FIG 48 Typical elevation of the RS T segment in acute pericarditis



FIG 49 Electrocardiogram of a patient with active rheumatic pericarditis (a) Elevation of the RS T segments at the beginning of the illness (b) typical inversion of the T waves later

The electrocardiogram in figure 48 was obtained from a 16 year old boy with active rheumatic fever and acute rheumatic pericarditis In addition to a sinus tachycardia one sees the marked upward displacement of the RS T segments This change is usually but not invariably most marked in lead II It is caused by

the inflammation of the superficial layers of the myocardium which had already been described by Virchow Experiments show that these changes appear even if a small area of epicardium with the underlying myocardium is damaged in certain places (Boyd and Scherf) The older view according to which these changes were the result of *extensive* alterations of the cardiac surface is incorrect

Figure 49 shows two electrocardiograms from a 35 year old woman with acute rheumatic pericarditis In figure 49 a the high take off' is visible in leads I and II Figure 49 b shows the characteristic next stage with the deeply inverted T waves *following a normal RS T segment*

Prognosis

Fibrinous pericarditis per se is not a cause of death but the development of *this complication in the course of another disease tends to make the outlook more* grave

Treatment

Therapy depends upon the nature of the underlying malady

SPECIAL FORMS OF FIBRINOUS PERICARDITIS

Nonspecific Pericarditis

This form also known as acute primary idiopathic benign or indeterminate pericarditis aroused considerable interest in recent years although it has been known for a long time

Nonspecific pericarditis occurs at all ages but is most common in adults It often follows an upper respiratory infection or pneumonia Pain occurring suddenly behind the sternum is a very common manifestation and it may be intermittent It may be aggravated by deep breathing swallowing or torsion of the thorax Sometimes the pain is severe enough to lead to shock In some cases the distress lasts for days The pain may be precordial and interscapular rather than substernal When pain is felt in the abdomen an acute abdominal *disease may be simulated Sometimes turning in bed greatly increases the severity* of the pain There is some dyspnea and cough moderate fever may persist for weeks The slightly increased sedimentation rate is associated with a mild leukocytosis (up to 10 000 leukocytes) Sometimes differentiation from an acute coronary occlusion is difficult in other patients differentiation from rheumatic pericarditis is necessary

A virus infection was postulated as the etiologic mechanism but this is not established Dressler suggested the possibility that an active rheumatic process is responsible

Roentgenologic examination shows a moderate enlargement of the cardiac shadow which may be the consequence of a pericardial effusion or myocardial damage

For therapy streptomycin chlortetracycline and oxytetracycline have been recommended The prognosis is excellent but the illness can be prolonged because recurrences (acute relapsing pericarditis) are common In recent years beneficial results from therapy with cortisone have been reported Transition of acute nonspecific pericarditis into constrictive pericarditis has been reported (Krook)

Rheumatic Fibrinous Pericarditis

Clinical rheumatic pericarditis may occur at any age but is unusual before the age of 5 and after 30 Most patients are between 8 and 20 years old Pericardial diseases generally speaking are more common in males than in females but no noteworthy differences have been noted in respect to rheumatic pericarditis

The symptoms have been described above but some points merit brief discussion Dyspnea is common and difficult to evaluate since nearly 50 per cent of the patients have an associated valvular disease Palpitation and indigestion may be the predominating symptoms Delirium is unusual in rheumatic fever but occurs in 12 per cent of those with rheumatic fibrinous pericarditis Bradycardia is not rare at the onset and is soon replaced by a tachycardia which may be out of proportion to the temperature The same holds for the very rapid respiration The white blood cell count and the sedimentation rate usually undergo no further increase as the result of pericardial participation in the general disease Serial electrocardiography often shows in addition to the features mentioned above prolongation of conduction time or dropped beats these findings are indicative of the myocardial involvement rather than being proof of a pericarditis

The outlook in children suffering from acute rheumatic fibrinous pericarditis is grave Not a few patients die from this complication while many who survive have some cardiac disability the life expectancy of nearly 25 per cent of those surviving the acute episode is less than five years The presence of an effusion or the presence or absence of a polyarthritis do not seem to affect the outcome Therapy with cortisone and ACTH greatly improves the outlook

An ice bag or cold application to the precordium is generally welcome since it reduces the pain and lessens the sense of palpitation Analgesics such as acetphenetidin may be tried Codeine is very useful since it abolishes the associated distressing cough Usually the salicylates are effective they may be required to render the general situation more tolerable and at times they add to the local comfort The value of any particular agent is difficult to assess since the course of the disease is exceedingly variable Large doses of salicylates particularly in the case of children seem to influence the course of the disease favorably

Uremic Pericarditis

This form of pericarditis originally described by Bright may occur in any disorder associated with azotemia The average age of affected patients is 35 to 37 years uremic pericarditis may be regarded as one of the commonest forms of pericarditis after the age of 30 years Males are affected more often than females

the ratio being 77 to 46 While any chronic renal disorder may be provocative chronic glomerular nephritis nephrosclerosis pyelonephritic contracted kidney and polycystic disease of the kidneys are usually responsible

The precise mechanism responsible for uremic pericarditis is unknown Culture of the pericardial fluid yields some organism in nearly 50 per cent of the cases but the organism varies from case to case the invasion is due to a terminal infection The intrapericardial injection of various constituents of the urine double ureteral ligation and double nephrectomy do not provoke pericarditis Some investigators believe that a failure of the liver to detoxify certain putrefactive products such as the phenols plays a part others stress the rather constant association of the pericarditis with necrotic lesions of the myocardium

Uremic pericarditis is usually asymptomatic and the diagnosis will often be missed unless a careful search is made for the friction rub whenever this complication is expected The discovery has prognostic significance — patients usually die within 3 weeks after its appearance although a few are reported to have survived for two or three months

The friction rub may be expected in approximately 10 per cent of the patients At first it is evanescent and faint then it becomes louder and more persistent but it may vanish with the appearance of an effusion

Fall of blood pressure sometimes occurs after the pericarditis becomes manifest The azotemia hypertension persistent acidosis the tendency to bleed into the skin and mucous membranes together with the abnormal findings in the urine make the origin of the pericarditis clear

Treatment is unsatisfactory and purely symptomatic

Tuberculous Pericarditis

The tubercle bacillus is capable of exciting all varieties of pericarditis Reference will be limited here largely to some points of general interest and a few features of the fibrinous form

Tuberculous pericarditis is not uncommon It may be expected once in every 100 necropsies in a general hospital and in approximately 4 per cent of all patients dying from pulmonary tuberculosis Although the disease occurs at all ages it is uncommon before the third year of life Approximately one third of the patients are less than 15 years old about one fourth are observed between the ages of 20 and 30 and over one third are observed after the age of 50 It has been estimated that 80 per cent of all cases of pericarditis after the age of 50 are tuberculous While these figures seem somewhat high to the present writers and seem to neglect the pericarditis following myocardial infarction they serve to emphasize that tuberculous pericarditis is not uncommon in the older age groups Males outnumber females in all reported series of cases (about 80 per cent of the cases are men) The disease is more common in Negroes and appears at an earlier age in this race A history of tuberculosis is often missing

Pericardial invasion is exceedingly common in the course of miliary tuberculosis and the incidence of pericardial involvement is greater than in other

serous membranes The rapidly evolving inflammation affects the epicardium principally and isolated tubercles may be seen along the coronary sulci

In many other cases the infection enters the pericardium by retrograde spread from a mediastinal tuberculous lymphadenitis At times the exact pathway can be followed along a connecting tuberculous lymphangitis Some believe that the subepicardial lymph nodes lying on the anterior surface of the aorta and those at the level of the atria and the peritracheal and peribronchial glands are originally affected so that they may be compared to the retro uterine catch basin in pelvic tuberculosis The existence of primary pericardial tuberculosis is exceedingly dubious

The exudative form is more common than the purely fibrinous one this term embraces serous *serofibrinous hemorrhagic and purulent tuberculous* pericarditis The incidence diminishes in the order named Often there is only slight inflammation macroscopically and the dominant disturbance is the huge hydropericardium In other cases the fibrin lies in stratified sheets sometimes with avirulent infections the organized fibrin is converted into a smooth white coat resembling the frosting on a cake

Another form is called nodular because of the large masses of granulomatous tissue when the nodules are numerous the gross picture may resemble that of a new growth

A rather common variety is termed caseous because a superficial layer of corrugated fibrin and of nonspecific granulomatous tissue covers caseating areas Between the zone of specific and nonspecific inflammation there is often a hemorrhagic effusion

The most common form is adhesive with partial or complete symphysis of the peri and epicardial membranes Moreover the outer aspect of the pericardium may become adherent to neighboring structures Sometimes the tissue becomes sclerotic and dense White fibrous tissue compresses the heart producing constriction This type is also called constrictive pericarditis

The clinical picture is so variegated that only general statements can be made In children the onset may be abrupt and difficult to interpret In adults there is often an insidious onset and the few cardiac symptoms are vague nausea vomiting diarrhea palpitation headache and similar symptoms may represent the chief complaints Nocturia eructations and epigastric fullness are mentioned with some degree of regularity Fever is an important symptom if the patient is aware of it Cough is often present but ordinarily is not mentioned unless it happens to be productive A relatively small number of patients have a sudden hemoptysis or blood streaked sputum owing to the associated pulmonary tuberculosis In a small number of patients night sweats loss of weight dull poorly localized chest pain and precordial distress may suggest the existence of pulmonary tuberculosis

Many patients fail to seek advice until the chest pain becomes severe Such pain is aggravated by exertion or deep breathing and is sometimes associated with blood streaked sputum Exertional dyspnea also often accounts for hospi

talization Ultimately the distress becomes constant and a sense of suffocation persists even at rest The ankles may swell the abdomen enlarges and the liver may become palpable so that cardiac failure seems a likely diagnosis This impression is heightened by the pale slightly swollen face A mild tachycardia extrasystoles or atrial fibrillation may be present Often the heart sounds are weak muffled and distant producing a tic tac kind of rhythm The friction rub is usually not heard unless paracentesis has been performed recently

That examination of the lungs frequently fails to disclose any abnormality seems rather surprising since the patient often seeks relief from the sharp stabbing pain in the region of the manubrium the supraclavicular region the neck or shoulder Physical examination discloses no explanation

If there are no suggestive features of tuberculosis in other areas the diagnosis of tuberculous pericarditis may present special difficulties The syndrome makes heart disease probable and only later will tuberculous pericarditis come under consideration This holds particularly for those cases in which dyspnea and weakness progress fever remains irregular or intermittent and evidence of pleural involvement is obtained Many of the symptoms just mentioned naturally belong to the effusion accompanying the pericarditis and are absent if the large effusion fails to develop

Four clinical types of tuberculous pericarditis are described in the aged (1) In the asthenic type the elderly individual rapidly loses weight and strength the evening temperature rises and the ankles may swell Syncope is a late symptom and often a precursor of death (2) In the uremic variety albuminuria hypertension and cardiac enlargement suggest a chronic nephritis if a friction rub happens to be present it is regarded as part of the uremic pericarditis Necropsy reveals a dry somewhat adherent tuberculous pericarditis with renal vascular athero sclerosis (3) In the pleuropulmonary variety dyspnea and cyanosis dominate while clinical examination of the heart reveals nothing abnormal The pulmonary pathology alone seems to explain the picture (4) In the cardiac form progressive dyspnea basal rales hepatomegaly and increasing edema suggest heart failure irregularities of the heart may add to the confusion The course is steadily downward and may be hastened by the development of pulmonary edema or by thrombophlebitis with pulmonary infarction Examination of the lungs fails to disclose an explanation for the dyspnea or cyanosis so that unless a friction rub happens to be present a false diagnosis of myocardial lesion is often made

The average duration of life in acute forms of tuberculous pericarditis with symptoms and signs of effusion formerly was about nine weeks There is a sub acute variety with predominant cardiac symptoms which evolves at a slower tempo — death may be postponed for two years In constrictive pericarditis of tuberculous origin several years may elapse between the onset of symptoms and death There is no doubt however that tuberculous pericarditis may be benign and self limited One wonders how many patients with benign 'virus pericarditis actually have this form

Therapy Great progress has been made in recent years and the mortality has been reduced with the application of streptomycin and isoniazid Thus the management of tuberculous pericarditis is not unlike that of tuberculosis elsewhere in the body

The morbidity and mortality rate is definitely reduced since therapy with isoniazid (or an equivalent agent) and streptomycin became available The ultimate results cannot be evaluated with finality at present but the early results are certainly much better In addition to isoniazid (300 mg daily) and streptomycin (2 grams every third day) some physicians advocate paraamino salicylic acid (12 grams daily)

Operative intervention is warranted in the constrictive type Formerly it was universally agreed that surgery should not be undertaken or if started should be interrupted if evidence of active tuberculosis is discovered With active infections death had been hastened or multiple fistulas formed after operation The situation has changed with the new therapeutic agents (streptomycin isoniazid) and some surgeons recommend pericardiectomy during an active tuberculous pericarditis (Mannix and Dennis) Since adhesions seem to develop much more rapidly under this therapy (Dubourg et al) early surgery in the form of pericardiectomy has been recommended

PERICARDITIS WITH EFFUSION

The diversity of etiologic factors capable of producing pericardial involvement was mentioned in the preceding section the same agents may cause pericarditis with effusion Pericardial effusions without pericarditis will be discussed later

Incidence Pericardial effusion is not rare (2 7 per cent of necropsies) The sexes are equally susceptible until the age of 20 years after which the incidence in females declines A vast majority of pericardial effusions occur before the age of 15 years (95 per cent) and a large number (60 per cent) are said to develop before the age of 5 (Blechmann)

Symptoms The general symptoms of this condition may be greatly modified by the special causative malady but the local symptoms are subject to less variation The speed with which an effusion develops determines part of the symptomatic picture and is also contingent to some extent upon the etiologic agent A rapidly developing effusion may produce signs of great urgency even if the amount of fluid does not exceed a few hundred cubic centimeters whereas a slowly developing effusion may be practically asymptomatic despite a high collection of fluid More than 2000 ml may be found in the pericardial cavity

Fever is usually but not necessarily present The temperature curve depends upon the type and intensity of inflammation and precludes the formulation of definite rules The temperature curve differs in serous and purulent exudates, tuberculous lesions and the like and there are too many exceptions to permit any generalizations

Other symptoms are similar to those seen in fibrinous dry pericarditis Thus pain may appear and may occasionally be of great severity The acute engorgement of the liver may cause pain in the right hypochondrium A large effusion may lead to pulmonary atelectasis and dyspnea

Since the chest wall fails to bulge when the pericardial effusion develops many of the local symptoms can be explained by the space occupying effect of the exudate

Inspection may reveal that the patient instinctively adopts a semirecumbent position often he is apprehensive obviously distressed pale or cyanotic With large effusion the sufferer may sit on the edge of the bed with the left arm elevated on pillows as if to provide extra space the cyanotic face the protruding eyes the cool forehead bathed in sweat the flaring alae nasi the extreme dyspnea and the scarcely palpable pulse paint an unforgettable situation

Bizarre positions were reported in patients with large pericardial effusions Thus the patient may assume the knee chest position or the posture of a praying Mohammedan

Signs Compression of the superior vena cava or the right atrium is common since the thin walled veins and atria must readily yield to high intrapericardial pressure The neck veins may be engorged and may fail to collapse in the upright position or in inspiration Edema of the face neck and upper extremities will be observed in patients with compression of the superior vena cava Inability of the cerebral veins to empty their contents may cause cerebral signs (faintness syncope)

The abdomen may protrude or the bulge may be limited to the upper abdomen when hepatic enlargement is responsible The liver becomes large and hard This event is facilitated by the fact that the wide valveless hepatic veins commonly are subject to direct compression by pericardial effusions owing to the supradiaphragmatic location of their orifices in the inferior vena cava (Elias and Feller) Moreover the liver may give the impression of being greatly enlarged since the pericardial effusion may cause the superior surface of the liver to rotate anteriorly The patients with large effusions and venous compression appear *markedly pale in contrast to the somewhat cyanotic hue noted in superior vena* caval compression the pericardial effusion diminishes the return of blood to the heart lowers the stroke volume causes the pulse to become small and frequently lowers the blood pressure

Palpation often reveals a small compressible soft pulse The heart rate is usually increased If irregularities are present they are due to the presence of associated myocardial damage The superficial layers of myocardium are always inflamed The apical impulse is often weak or impalpable Cardiac pulsations may be felt however, even in the presence of a large effusion if it develops for the most part posteriorly A friction rub may be palpable despite the collection of considerable pericardial exudate The upper border of the first rib may become palpable this is called the first rib sign of Ewart The findings over the lungs vary

with large effusions which compress or displace the lungs vocal fremitus may disappear from the left paravertebral area

Percussion yields more important information Early the area of relative dullness becomes flat and merges with the area of absolute dullness and the transition from the area of dullness to normal pulmonary resonance may be very distinct Percussion reveals more than the usual dullness found over an enlarged heart There is absolute flatness which is very characteristic and which often permits the diagnosis even of small amounts of fluid when other methods fail to disclose its presence In 1761 Auenbrugger described the percussion sound in pericardial effusions as being completely dead as if percussion were applied to a fleshy limb We cannot stress strongly enough the importance of this sign

At one time great emphasis was placed upon the change in the cardiohepatic angle from acute to obtuse This sign has been proved valueless for x ray examination shows that an acute cardiohepatic angle may be present with all types of effusion

The shape of cardiac dullness varies when pericardial effusion is present If the effusion forms around a heart whose configuration is abnormal owing to some old valvular lesion the pericardial silhouette may retain its configuration Thus a mitralized heart will remain mitralized an aortic heart retains its aortic form (Zdansky) Moderate pericardial effusions often expand cardiac dullness to the right so that the area seems triangular The symmetrical expansion far into the right and left lung fields with the small vascular band on top (figure 51) causes a shadow that has been compared to a Hottentot s hat or to a water bottle the right and left cardiac borders just beneath the vascular band may proceed almost horizontally for a few inches

Dullness in the fifth right intercostal space parasternally so called Rotch s sign is common There is also widening to the left but sometimes this is difficult to determine by percussion when a left pleural effusion coexists In a few patients the diagnosis is suggested by the demonstration of the apical impulse within the area of cardiac dullness ordinarily the apical impulse is the most lateral and caudad point of dullness

Percussion of the posterior aspect of the chest may provide additional information Frequently there is dullness in the lower left posterior chest this has been named the posterior patch of pericardial dullness Frequently this sign is demonstrable in children and may be associated with a small area of tubular breathing and egophony at the angle of the left scapula

In typical cases the heart sounds are faint and muffled however a friction sound may be audible despite the presence of a large effusion when the fluid collects posteriorly and presses the heart near the surface of the chest This also explains why powerful cardiac pulsations may be felt why the sounds and murmurs may be loud and why the classical silent heart is absent Under these conditions confusion of a pericardial and myocardial disease is likely In some instances the pulse vanishes with inspiration (pulsus paradoxus) (see later)

A vast number of additional signs are present in a few cases they owe their origin to pressure upon various neighboring structures Since they are encountered in relatively few patients no detailed description is necessary but a few may be mentioned since they may dominate the clinical picture Dysphagia may be the outstanding symptom when the effusion compresses the esophagus or tormenting cough or hiccough may harass the patient Involvement of the recurrent laryngeal nerve may produce voice changes and pressure upon the sympathetics may inaugurate a number of eye signs

Diagnosis The above account of the physical signs is not intended to suggest that the diagnosis of a pericardial effusion is always easy In about 25 per cent of the cases the friction rub is audible from the start so that the evolution from a fibrinous pericarditis can be followed often the presence of some symptom complex like a tuberculous polyserositis or tuberculous peritonitis will cause the examiner to pay special attention to the heart Under these circumstances little difficulty is encountered On the other hand the effusion may develop insidiously in the course of months or years and subjective complaints are absent or minimal for a long time In these cases the diagnosis may be missed

Not rarely the patient seeks relief from upper abdominal pressure produced by the enlarged liver Pressure on the superior vena cava causes discomfort in the neck and slight dyspnea A suggestion of the correct diagnosis may be furnished when the patient unconsciously adapts the sitting position with slight inclination to the left or forward and the left arm elevated on pillows When the heart is examined the physician may be amazed to discover an enormous increase of cardiac diameters Often the disproportion between the enormous size of the heart and the relatively slight discomfort of the patient leads to the correct diagnosis

Roentgen Examination and Electrocardiogram An x ray film will show the enlargement of the cardiac shadow mentioned before With a simple chest plate an enlargement due to a valvular lesion or a myocardial lesion cannot be not ruled out Thus the form of the heart shadow in figure 50 a which was obtained from a 53 year old man with tuberculous pericarditis is like the one commonly found in a combined rheumatic mitral and aortic valvular lesion or in a patient with hypertension or coronary sclerosis with left ventricular failure and pulmonary congestion Figure 50 b was obtained two weeks later and shows the disappearance of the effusion Pulmonary congestion has also vanished

The more characteristic water bottle appearance of a very large effusion is visible in figure 51 obtained after a paracentesis with the removal of about 400 ml of exudate and the injection of some air into the pericardial cavity This causes a horizontal fluid level and makes the upper left portion of the pericardium visible

On fluoroscopy the complete absence of pulsations at the cardiac borders is often decisive for the diagnosis To be sure in rare instances pulsation of the cardiac borders is not perceptible in extremely severe myocardial damage however in the latter instance the patient displays very obvious evidence of advanced

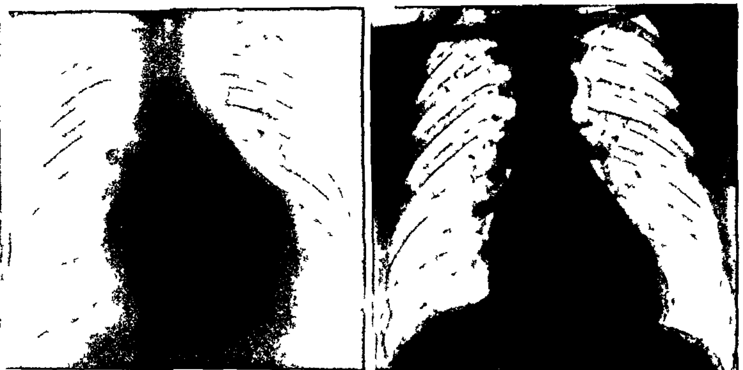


Fig 50 Exudative pericarditis before (a) and following (b) absorption of exudate

decompensation With effusion the still cardiac borders are surrounded by remarkably light lung fields since the stasis occurs back of the heart so that the lungs are free from congestion This does not hold when there is additional failure of the left ventricle for then pulmonary congestion may appear

The diagnostic situation may be complicated by the fact that effusions are sometimes encapsulated If the residual encapsulated exudate is associated with

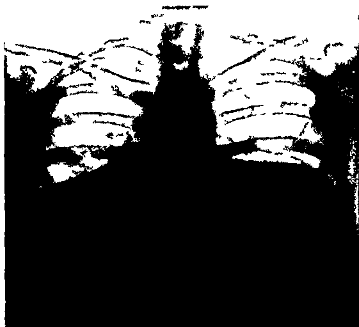


FIG 51 Pneumohydropericardium

low grade persistent inflammation and low pressure a chronic inflammatory pericardial diverticulum may form This encapsulation is prone to occur along the right border of the heart and in contrast to valvular lesions tends to distort the right edge of the cardiac silhouette One may also observe peculiar globular shadows *the size of a plum or larger in this area when they are multiple* peculiar hexagonal irregular shadows may be visible

Fluoroscopy is more important than films because these loculated effusions often change their shape during the different phases of respiration moreover this method permits the observations of local pulsation in the bulging area The clinical silence of many of these encapsulated effusions is the reason for their belated discovery

Other Tests Angiocardiography may be very useful for establishing the diagnosis The cardiac shadow filled with the opaque agent is seen surrounded by the less opaque shadow caused by the effusion

The electrocardiogram often but not invariably shows low voltage The I and T waves may disappear completely

Great variability prevails in the laboratory findings particularly in respect to the sedimentation rate the white blood cell count and similar findings Whether or not they are altered and if so to what extent depends upon numerous factors indicated in the discussion of the etiology of pericardial effusions

Paracentesis The diagnosis of a pericardial effusion can be established by a test puncture this procedure is not recommended in the presence of an encapsulated effusion because of the increased risk of damaging the myocardium in such cases

Differences of opinion prevail regarding the most suitable place for paracentesis As with puncture of the pleural cavity it is unwise to adhere to inflexible rules The special circumstances of the individual case vitally influence the decision Parasternal puncture should be avoided because of the possibility of injury to the internal mammary artery Generally speaking any paracentesis to the right of the sternum is dangerous since the thin walled atrium may be punctured Paracentesis in the fifth or sixth interspace 6 to 7 cm lateral to the left border of the sternum is recommended With large effusions a site of puncture outside of or below these points may be selected Likewise paracentesis from behind (especially worthy of recommendation for posterior effusion and for simultaneous pleural effusion) and from below (between the xiphoid process and the left costal margin) is often advocated The latter is frequently called the Marfan method

It is advisable to employ local anesthesia (novocaine) It is also advisable to insert the needle detached from the syringe since in this way the resistance of the skin and musculature are appreciated more readily and the entry of the needle into free space is recognized more easily Puncture of the ventricular muscle should be avoided although the dangers of this accident are overemphasized by many The direction of the needle will vary with the site selected for puncture At the place recommended left lateral puncture it is inward backward and upward

The electrocardiogram may be used as an additional safeguard during paracentesis (Bishop et al) When the needle touches the myocardium an elevation of the PS T segment appears in a special lead the needle serving as one electrode

The character of the fluid removed may provide some diagnostic hint of the nature of the process although this information is not always reliable Thus serous fluids are infrequent in infections with pathogenic cocci bloody fluids are often encountered in tuberculous pericarditis and neoplasms Sometimes the provocative microorganism may be recovered but it should be borne in mind that the original organism may be overwhelmed by secondary invaders Apart from the establishment of the diagnosis of an effusion paracentesis has value in eliminating the prospect of a pyopericardium and in lowering intrapericardial pressure

Treatment The management of these patients depends to a great extent upon the etiology Therapy of rheumatic or tuberculous pericarditis has been discussed above

There is justification for the use of sulfonamides in the treatment of pneumococcus pericarditis with effusion since these substances readily diffuse into the pericardial cavity Formerly the oral administration of these drugs was combined with the intrapericardial injection of specific antisera Before much experience was obtained on the value of this combination the use of penicillin gained prominence This method of therapy is indicated in pericarditis evoked by the various pathogenic cocci Broad spectrum antibiotics are also of value There is however the danger that a nonpurulent effusion produced by these organisms may become rapidly converted into a pyopericardium The superiority of surgical intervention over conservative measures in the latter condition makes it necessary to follow the patient very carefully whenever the etiology of the pericardial inflammation suggests the possible development of a pyopericardium As a general rule the situation calls for very careful evaluation of the microorganisms recovered from the pericardial fluid

Apart from these etiotropic measures some comfort may be provided by symptomatic treatment If relief of pain comes under consideration the suggestions made in the section of fibrinous pericarditis are worthy of trial Digitalis and allied preparations are rarely indicated in pericardial effusions and in the absence of cardiac decompensation may act unfavorably

The therapeutic program must also be considered from the standpoint of how quickly the effusion developed If the exudate forms rapidly and causes a marked increase of intrapericardial pressure and severe inflow stasis early puncture and removal of fluid are necessary In large chronic effusions in which the inflammatory or infectious process stands in the background a more conservative plan may be adopted Occasionally success is obtained by means of a mercurial diuretic in combination with ammonium chloride at times a jolt with theophyllin may bring about absorption of the effusion Frequently however these measures are of no avail and paracentesis must be resorted to

It should be emphasized that the quick removal of a large amount of pericardial fluid may be associated with danger If the heart has been subjected to the pressure of the effusion for a long time and if the myocardium has been injured by the accompanying myocarditis and the compression rapid release of the pressure and the acute increase of demands on the heart by the suddenly heightened influx of blood may result in acute cardiac dilatation syncope and the manifestations of severe failure which at times may be fatal The distended pericardium cannot like the normal pericardium prevent excessive cardiac dilatation For these reasons we advocate the use of a 20 ml syringe for the removal of large effusions and slow withdrawal of the fluid Each time the syringe is disconnected for emptying 10 ml of air are reinjected through the needle to prevent an acute reduction of pressure In rheumatic pericarditis it is often well to postpone paracentesis in the absence of definite indications for fairly large effusions are often absorbed in 3 to 4 weeks

In many forms of effusion the relief afforded by pericardial paracentesis is only transient as the fluid rapidly reforms Moreover the effusion may be ab

sorbed very slowly and the clinical picture may gradually change from one of effusion to that of pericardial adhesions Very often the myocardium has suffered permanent damage and cardiac failure ultimately develops Various operative procedures the drainage of pericardial fluid into the pleural cavity or pericardiectomy have been suggested but have not found widespread adoption

The situation may be further complicated particularly in patients with tuberculosis by the development of a polyserositis Sometimes these patients present obvious evidence of progressive tuberculosis with effusions into the pericardial pleural and peritoneal cavities — Concato s disease in a strict sense On the other hand pericardial effusion may be minimal or absent while early ascites (ascites praecox) hepatomegaly or recurrent pleural effusion characterize the clinical picture These cases are often called pericarditic pseudocirrhosis or Pick s disease and they are discussed in the chapter on pericardial adhesions

SUPPURATIVE PERICARDITIS (PYOPERICARDIUM)

Although the symptoms and signs of purulent pericarditis may depend upon pressure effects and thus may resemble those of nonpurulent pericardial effusion it seems advisable to discuss pyopericardium separately in order to emphasize that the toxic and infectious phenomena may dominate the situation while pressure effects stand far in the background

Etiology In general acute purulent pericarditis may be considered a more intense response of the pericardium to the same etiologic agents which cause the forms of pericarditis previously discussed The intensity of the stimulus seems more important than the nature of the pathogenic agent It must be admitted however that rheumatic pericarditis is rarely purulent (Gerke) whereas pneumococcic pericarditis tends to be suppurative in a large number of cases

Purulent pericarditis was exceedingly common during the great pandemic of influenza in 1917 — 18 in one series of patients 14 5 per cent of individuals dying from pneumonia had pyopericardium (Stone) Bacteriologically proven pyopericardium due to the influenza bacillus is rare but a complicating streptococcic pyopericardium in influenzal pneumonia is very common In most cases of pyopericardium some intrathoracic infection is present usually this is pneumonia with or (rarely) without empyema In 77 of 123 cases of purulent pericarditis there was intrathoracic infection Among these the pneumococcus was provocative in 45 the staphylococcus in 17 and a streptococcus in 3 (Bisgard)

Pericarditis complicating sepsis is usually purulent This is true almost invariably for the pericarditis following peritonsillar abscess A major source of pyopericardium is sepsis associated with osteomyelitis Among 71 cases of acute osteomyelitis 51 came to necropsy and a purulent pericarditis was present in 33 The lungs were affected in 22 and an empyema or pleuritis was present in 10 18 had abscesses of the kidneys (Pyrah and Pain) Puerperal sepsis furnishes a fair number of examples of pyopericardium

Most of the pathogenic cocci are capable of producing purulent pericarditis Apart from purulent pericarditis as a serious incident in the course of pneumo staphylo or streptococcic sepsis some specific diseases may be associated with pyopericardium Gonococcic pericarditis though rare is often purulent and is almost invariably associated with endocarditis of the same origin Meningococcic pericarditis which occurs in a dry as well as a purulent form is more common since patients survive the acute phase because of the use of antibiotics Bacilli are less prone to produce purulent pericardial lesions Thus typhoid pericarditis is actually uncommon and other organisms of the same group (colon paratyphoid salmonella) are rare causes Actinomycosis may produce a typical pericarditis which is often purulent in character Among the higher organisms the amoeba may enter the pericardial cavity In these cases there is usually a fistulous connection to a liver abscess and examination of the chocolate colored pericardial fluid usually reveals a mixed infection

Incidence Pyopericardium is not common a year may pass without a single example being noted in a large hospital The incidence of purulent pericarditis mentioned in the literature depends upon the source of the material If it is stated that purulent pericarditis is twice as common as the combination of all other forms of pericarditis with effusion the indication is that the material from which the statistics were compiled was predominantly surgical

A vast majority of cases are observed in older children and young adults The disease is not common before the age of five and is equally unusual after the age of 25

Pathology The pathologic picture of purulent pericarditis depends to some extent upon the stage of the process An early serofibrinous stage is followed by the formation of fibrino purulent exudate The surface of the membranes becomes cheesy and soft pure odorless pus forms in variable quantities or a hemorrhagic and purulent exudate is found The inner aspect of the pericardium often resembles a purulent granulating wound with a pyogenic membrane Cardiac movements usually preclude the formation of many adhesions although constrictive pericarditis may follow a purulent inflammation Sometimes the pericardial exudate undergoes considerable organization and massive deposits may attain a diameter of several centimeters More often the pericardium is damaged with the result that remarkably large amounts of fluid collect

Symptoms The symptoms vary because of the diversity of etiologic factors Generally there is an acute illness with swinging temperature chills profuse diaphoresis and evidence of toxicity The diagnosis may be missed because the underlying disease may seem adequate to account for the symptoms therefore no search is made for a second disease or a complication Moreover the development of a purulent pericarditis need not change the general symptoms to a great extent Actually the tendency for pericardial suppuration to remain latent is notorious

Signs Inspection does not give much assistance Most patients present signs ordinarily associated with an elevation of temperature but in rare cases the tem

perature may be normal The respiratory rate and dyspnea may be disproportionately great If the volume of pericardial fluid is large the patient may assume a semi recumbent posture Bulging of the precordium is rare even in children

Palpation percussion and auscultation reveal the same findings as in non purulent pericardial effusion The skin over the precordium is often edematous

There are all gradations of symptoms and signs The clinical picture in the patient whose pleural empyema extends to the pericardium will be different from the one in the patient whose purulent pericarditis results from sepsis with hematogenous dissemination of bacteria (e g when osteomyelitis causes a small myocardial abscess which subsequently ruptures into the pericardial cavity) If the effusion is large tamponade may result Under these conditions the neck veins distend the pulse becomes small rapid and irregular and other evidence of cardiac compression develops With small effusions the area of cardiac dullness does not enlarge although slight edema of the chest wall or of the upper thorax may be seen

The disease is recognized most often when the possibility of its existence is constantly borne in mind in the presence of a process capable of producing pyopericardium Since the existing fever leukocytosis and sedimentation rate need not undergo further alteration when purulent pericarditis develops careful repeated examination of the precordial area is of great diagnostic value If the examiner lacks the necessary experience to detect the flatness in the area of cardiac dullness serial x ray films may furnish a guide to the recognition of the malady

Diagnostic pericardiocentesis is considered unjustified by many competent observers Much of the adverse judgment arises from a period when such puncture was employed as a therapeutic rather than a diagnostic measure Pericardial paracentesis in these patients is not entirely devoid of danger although its hazards are frequently overemphasized by its opponents It is true that the passage of a needle through an infected pleural cavity into a sterile pericardial cavity may be costly or conversely that infection of the pleura during paracentesis of a pyopericardium is also possible The production of a myocardial abscess or a cardiac laceration by an infected needle although rare does occur On the other hand the pleura is usually adherent over the site of puncture and pleural empyema seems to be a greater theoretical danger than an actual one However despite these facts we usually perform pericardial paracentesis if there is any doubt about the situation In this connection it must be admitted that sometimes no pus is recovered even though it is actually present moreover the pus obtained may be ascribed to a pleural rather than a pericardial empyema The danger of overlooking a purulent pericarditis is so great that it seems advisable to err on the side of safety and to perform an occasional unnecessary pericardial tap

Course The course of the disease varies remarkably If the tempo is fulminating cardiac tamponade may occur within a few days on the other hand pyopericardium developing in connection with a foreign body in the pericardial cavity or after a shrapnel wound in the lung may appear late Transmission of infection through the pericardium is sometimes slow

Prognosis In the past under medical treatment fatalities amounted to almost 100 per cent After pericardiotomy became popular this figure was lowered to about 42 per cent (Truesdale) Just before the antibiotics became popular the death rate for pneumococcic pyopericardium (37 per cent) streptococcic infections (31—50 per cent) and staphylococcic pyopericardium (25—34 per cent) was still high, at the present time it has however apparently been reduced decidedly although no large statistical series is available for comparison The antibiotics readily pass into the pericardial cavity in effective concentrations Still the death rate remains high in pyopericardium especially if surgery comes too late

Treatment If pericardiocentesis is performed several syringes should be available to evacuate a fairly large amount of fluid in the event pus is present About one half as much air should be reinjected for in addition to the reasons given above the pneumopericardium greatly facilitates the recognition of any *encapsulated exudate by x ray and may modify any operative procedure*

Pericardiotomy is indicated even with the modern antibiotics in most cases A few hours of delay before operation is permissible in order to make proper preparation of the patient but next to nonrecognition of the disease procrastination remains a very large factor in the fatal outcome Operation is futile if a pleural empyema or encapsulated pericardial pus is overlooked Momentary reflex stoppage of the heart on incision of the pericardium is a rare but extremely serious occurrence It can usually be avoided by the application of novocaine to the membrane before incision

The administration of antibiotics presents no special problems Many such drugs can be applied locally as well as by other routes

GANGRENOUS PERICARDITIS

Etiology The entrance of putrefactive organisms into the pericardial cavity through a penetrating wound or after perforation of a bronchogenic carcinoma may produce necrosis of the pericardium Pyopneumopericardium is a common result

We have seen gangrenous pericarditis follow the perforation of an esophageal traction diverticulum into the pericardium and similar catastrophes after the implantation of radium into an esophageal carcinoma More rarely we have observed a tuberculous cavity of the lung penetrate an adherent pericardium The greatest number of cases however is provided by penetrating wounds of the chest

Pathology Sometimes the parietal pericardium is smooth and shiny but more often it forms a rigid shell which retains its shape after the heart is removed from the cadaver The visceral layer looks as if tiles had been laid in soft cement Frequently a fistula can be found leading to a bronchus and the foul pericardial content may have been largely evacuated in this way

Symptoms and Signs Most clinical features are described under the heading Pneumopericardium

NONINFLAMMATORY PERICARDIAL EFFUSIONS

Hydropericardium (Hydrops Pericardii)

Congestive Heart Failure The moderate increase of pericardial fluid often found at necropsy in congestive heart failure is usually devoid of clinical significance On occasion however for unknown reasons large effusions cause a marked enlargement of the cardiac shadow in some of these cases Usually they respond readily to treatment with diuretics

Beriberi Scurvy Among 64 cases of oriental beriberi Wenckebach noted a pericardial effusion in 62 hydrothorax in 14 and ascites in 9 Stasis and hypertension in the venous circulation as well as low plasma proteins are considered responsible for the transudation of fluid in this disease Myocardial damage is also present

This effusion explains the striking variations in the cardiac size of the affected patients *Hydropericardium does not seem to have been noted in the occidental* beriberi heart

Other vitamin deficiencies do not seem to produce pericardial disturbances The epidemic pericarditis encountered in war prisoners in 1918 was due to hemopericardium resulting from scurvy and not from an inflammation

Myxedema Another form of hydropericardium of interest to the internist stems from myxedema This form will be described in the section on endocrine diseases There is also a form of hydropericardium in which the pericardial fluid contains large amounts of cholesterol in an otherwise clear fluid It is asserted that despite the absence of other signs of myxedema these patients respond favorably to the administration of thyroid extract Pericardiectomy has also been recommended (Creech et al)

Pericardial fluids with a high content of cholesterol are also found in tuberculous pericarditis with effusion but under these conditions the fluid is opaque and often chocolate colored

In rare cases we have seen a large transudate in the pericardial cavity of otherwise fully compensated patients without any detectable etiology

Hemopericardium

Individual causes of hemopericardium are mentioned in several places in the present book but may be summarized briefly at this time The normal heart may be ruptured by a crushing thoracic injury or by a fall from a great height this is frequently observed in fatal airplane crashes Rupture of a diseased heart is not a rare event after coronary thrombosis with myocardial infarction In recent years perforation of the atrium by an extension of a bronchogenic carcinoma has been observed with increasing frequency

Fatal cardiac tamponade has been observed after sternal puncture

Rupture of the intrapericardial part of the normal aorta occurs in aviation catastrophes and is sometimes seen in steering wheel accidents when an automobile driver is thrown forcibly against the steering wheel A hemopericardium

developed in a 23 year old man who received a severe blow on the chest during a foot ball game Four and one half pints of blood were removed and the patient recovered

The pathologic aorta often ruptures in aneurysms when the intrapericardial portion of the thoracic aorta is affected Dissecting aneurysm associated with media necrosis is likewise a common cause A normal coronary artery may be perforated in a stab wound similar accidents have happened during paracentesis or intracardiac injections In a vast number of instances an atherosclerotic coronary artery ruptures into the myocardium rather than into the pericardial cavity Aneurysms of the coronary artery are uncommon they occur in the form of congenital miliary aneurysms as well as in periarteritis nodosa Injuries and rupture of the pulmonary artery with leakage into the pericardial cavity are relatively rare however hemopericardium may follow stab wounds of the vessel

Hemopericardium may result from capillary bleeding in scurvy nephritis acute leukemia and many other diseases of the blood forming organs

Hemorrhagic pericarditis is a term employed to describe rather intense pericardial reactions to an inflammatory stimulus Ordinarily it represents a more severe reaction than serofibrinous pericarditis and its etiology is equally diversified

Pericardial tumors are rare (see below) but a times they produce hemopericardium

The symptoms and signs of hemopericardium depend upon the etiology the speed with which bleeding occurs the amount of blood which escapes into the pericardial cavity and the presence or absence of cardiac tamponade Uninfected blood in the pericardial cavity is absorbed with considerable speed whereas infected blood is rapidly converted into a purulent liquid

Chylopericardium

True chylopericardium is exceedingly uncommon but pseudochylous effusions are frequently encountered in the pericardial cavity We have noted chylopericardium in conjunction with injuries of the thoracic duct Granuloma and new growths involving the duct may also be responsible Experimental chylopericardium can be produced in some animals by ligation of the superior vena cava but it fails to appear after thrombotic occlusion of the same vessel in man

Even more rare is *cholopericardium* the appearance of bile in the pericardial cavity (perforated liver abscess)

Pneumopericardium

Etiology Uncomplicated pneumopericardium is practically unknown for the entrance of air into the pericardial cavity is almost invariably associated with the appearance of blood or some other fluid mixed forms rather than pure forms of pyo hemo pneumopericardium occur

The greatest single etiologic factor is trauma (James) In addition to injury in the usual sense (contusion of the chest wall with and without fractures pene

tration of the chest wall by foreign bodies wounds) air may enter via a perforated esophagus (splinter of bone fish bone for example) We saw pneumopericardium in a patient who swallowed his dentures They were found in the middle of the esophagus The penetration of a tuberculous pulmonary cavity or inflammation arising in a tuberculous lymphadenitis or a bronchogenic carcinoma repre ent other mechanisms Equally common however though often unappreciated is the pneumopericardium which follows attempted pleural paracentesis for the induc tion of pneumothorax Pneumopericardium may follow tracheotomy or pneumo mediastinum

Clinical Picture The manifestations are variable as might be expected from the multiplicity of etiologic factors The speed with which air enters is a factor in the production of symptoms a tension pneumotamponade may create symp toms whereas a larger but open wound may avert a rise of intrapericardial pressure

Ordinarily inspection reveals little unle s the trauma or some other releasing factor produces the symptoms of shock Larger collections of air may cause dyspnea tachycardia and sharp precordial pain but small amounts may not even cause engorgement of the jugular veins Palpation is likewise often uninform ative Obliteration of the apical impulse is commonly reported Percu sion may yield a tympanitic or metallic note in place of cardiac dullness or flatness The metallic component of the sound is important since it excludes mediastinal emphysema as the provocative factor This tympany may be difficult to detect when it merges imperceptibly with the surrounding resonance of the normal lung Sometimes a classical cracked pot sound (bruit du pot fele) is obtained on percussion

Auscultation yields diagnostic information A splashing ringing metallic sound synchronous with the heart is audible This continuous Hippocratic succus sion sound is heard in approximately half of the cases The preci e characteristics of these sounds will depend upon the amount of air and fluid present the size of the fistulous opening pericardial tension etc

The mill or water wheel murmur (bruit de roue hydraulique) is almost pathogno monic This sound is difficult to describe and is usually compared to that of a churn It may be louder on in piration than on expiration and may vary in inten sity from time to time for no apparent reason Stokes de cribed the phenomenon as a large crepitating and a gurgling sound to which was added a distinct metallic character Often there is a loud tinkling synchronous with the heart sounds which can also be heard at a distance from the patient The heart sounds as well as the friction rub if present have a metallic character

The clear gas filled space demonstrable around the cardiac shadow and the surrounding bands of pericardium create an unmistakable x ray picture The upper level of the pericardial effu ion is clearly demarcated by air The thickness of the pericardium is easily estimated If a productive tuberculosis is responsible for the accident the pericardium is visible as a den e ligamentous curved band on each side just above the pericardial effu ion

Differential Diagnosis The principal difficulty lies in excluding pneumomediastinum In addition to the distinguishing signs mentioned above metallic tinkle is important since this is usually absent in pneumomediastinum Subcutaneous emphysema is often but not invariably present in pneumomediastinum Fine crackling sounds synchronous with cardiac movements are also suggestive of pneumomediastinum

In patients with pneumothorax the mediastinal pleura may assume the appearance of an arc and may resemble a pneumopericardium Usually the extremely active movements of the heart so typical of pneumopericardium under the fluoroscope are absent

Prognosis Most of the patients recover All forms of pneumopericardium which became secondarily infected were associated with a poor prognosis before the antibiotic era

Treatment Simple collections of air are rapidly absorbed although the patient must be watched carefully If air causes tamponade paracentesis should be performed this applies in all forms of tension pneumotamponade If the air and fluid reform surgical intervention is usually necessary

PERICARDIAL ADHESIONS

The epicardium and pericardium may adhere to each other or the outer aspect of the pericardium may become adherent to neighboring structures as the result of acute or chronic pericarditis Since these events may take place in any form of pericardial inflammation in which repair is associated with fibrosis practically all forms of pericarditis may be causal

Nomenclature

Due to the fact that the presenting situation is usually a postinflammatory syndrome rather than an active inflammation the terms concretio cordis and accretio cordis have become popular The phrase adhesive pericarditis should be discarded since in most cases we are not dealing with an active inflammatory process In concretio cordis the epicardium and pericardium become connected all grades exist between the single fibrous strand bridging the pericardial cavity to the complete obliteration of the sac The term accretio cordis on the other hand emphasizes the adherence of the pericardium to the surrounding structures and is used more or less interchangeably with mediastinopericarditis Important too is a particular form of concretio cordis in which the pericardial scar compresses the heart In some progressive cases usually tuberculous in origin the term constrictive pericarditis is justified but in others the inflammatory lesion has long since subsided and the syndrome is due to chronic cardiac compression by the pericardial scar

Incidence Etiology

Pericardial adhesions are found in approximately 5 per cent of routine necropsies about 48 per cent of patients dying from pericarditis have adhesions

The etiology as indicated earlier is extremely diverse For practical purposes one third of the cases are rheumatic in origin but it is rare for the scar of rheumatic pericarditis to produce cicatrices of clinical importance Many of these patients have no evidence of associated valvular disease Pericardial adhesions presented by another third of the cases may be considered tuberculous in origin It has been repeatedly asserted that all instances of chronic cardiac compression by pericardial adhesions are due to tuberculosis This would appear to be correct if the phrase pericardial adhesions is used synonymously with the syndrome about to be described To be sure an occasional instance of this syndrome has followed a pyopericardium of streptococcic origin but it is difficult to overemphasize the importance of tuberculosis in the genesis of symptom producing concretio cordis Its role in the production of mediastinopericarditis is also so great that it scarcely requires discussion In rare cases the pericarditis followed trauma to the chest

Pathology

As indicated above the scar may consist of a band or a plaque or it may completely obliterate the pericardial cavity There is a growing inclination to distinguish the pathologic changes in the constrictive type from those in the nonconstrictive Thus it is stressed that in the constrictive type the pericardium is thicker more dense and tougher for the fibrous tissue has undergone complete hyalinization The closely bound enormously thick individual collagen fibers are swollen structureless of glassy translucent appearance and without internal architecture The fibers are parallel for the most part but they may form interwoven systems of dense whorls Apart from a few linear nuclei outside the hyaline fibers the scar is almost acellular The tissue is strikingly devoid of capillaries although it may contain some large blood vessels

While this picture is present in many cases others have areas of caseous debris residual old hemorrhages spaces formerly filled by collections of cholesterol crystals calcification of various degrees and extent Sometimes the old line of cleavage between the two layers of membrane has been preserved by a small collection of pus Usually no organisms can be demonstrated although they may be recovered by cultures Sometimes tubercles are found

Pathologic Mechanism

The existence of a pericardial adhesion or for that matter of obliteration of the pericardial cavity does not necessarily result in symptoms On the contrary some adhesions at the site of an old myocardial infarction may support the scar and may perhaps provide an important source for a new blood supply Likewise complete adherence of a thin flexible pericardium to the epicardium may not hamper cardiac movements any more than a thin rubber glove restricts the movements of the fingers On the other hand a thickened pericardial callus encircling the heart may prevent diastolic relaxation and emptying of the great veins In the same way adhesions between the pericardium and neighboring structures the anterior chest wall for example may angulate or rotate the heart and thereby

produce symptoms or signs Systole may also be hampered by the adhesions Accordingly no symptom or sign is obligatory in the clinical picture associated with pericardial adhesions rather it is the total impression that is suggestive In the following discussion no attempt will be made to distinguish concretio and accretio cordis clinically since they are usually combined However a brief review of the classical constrictive type may serve as an introduction

Cardiac catheterization has revealed an elevation of arterial pressure in the lesser circuit that disappears after cardiolysis The right ventricle is hypertrophied The right heart pressure patterns are characteristic but not pathognomonic The right atrial pressure curves show an M or W form and the right ventricular curve shows an early dip and a plateau formation because of incomplete diastolic filling Electrokymography shows a flat top pattern Myocarditis or amyloidosis of the heart may lead to similar curves

Since the encircling pericardial scar prevents diastolic relaxation of the heart and the inflow of blood from the superior and inferior vena cava is drastically affected the picture presented is one of congestion affecting the tributaries of the superior and inferior vena cava The engorged neck veins are unable to empty and remain filled even during inspiration The hepatic veins are unable to discharge their contents so that the liver enlarges and ascites appears early Since the myocardial fibers undergo considerable atrophy and diastolic relaxation is greatly reduced the heart tends to be small although the thickness of the callus may make the diameters seem approximately normal on x ray films In most patients there has been no antecedent valvular lesion with the result that no murmurs are heard The heart sounds are often weak causing the precordium to appear as quiet as a church

Symptoms and Signs

Dyspnea is a common symptom and occurs only on exertion Frequently the patient complains of increasing weakness The enlargement of the liver is so insidious that pain in this area is uncommon but a sense of fullness or oppression in the upper abdomen develops sooner or later in most patients Most of those afflicted with constrictive pericardial scars seek relief for noncardiac symptoms and although the situation strongly suggests some form of heart disease strikingly little is found to confirm this impression Superimposed on the diagnostic triad engorgement of the neck veins enlargement of the abdomen and a small rather silent heart there may be a host of signs some of which are mentioned below

Inspection This may reveal some edema of the slightly suffused or cyanotic face The edema as well as the cyanosis often stop abruptly at the neck (Stokes collar) The facial edema is most pronounced in the morning and disappears during the day when the patient is up and the inflow of blood from the head into the heart is facilitated The neck veins are distended and under great tension as shown by measurement of the venous pressure Other veins may not show obvious engorgement although pictures taken by means of infrared photography also reveal dilated cutaneous veins throughout the body

In the past great emphasis has been placed upon abnormal movements in the cardiac and other areas. Weakness or absence of the apical impulse was formerly considered an important sign although it is now recognized that the impulse is frequently absent in normal subjects and may persist despite the presence of extensive pericardial adhesions. Systolic apical retraction may occur with properly located adhesions; a forward movement in the same area may be noted in other patients. But both signs also occur without adhesions. Among the thoracic movements which have received great attention is Broadbent's sign, a systolic retraction produced by adhesions in the left axillary line in the vicinity of the eleventh and twelfth ribs; it is supposed to be suggestive of posterior mediastino-pericardial adhesions but is in most cases absent. Moreover, it also occurs in other diseases. Suitably located adhesions may produce retractions in other areas, usually on the anterior chest wall. Often the systolic retraction of the interspaces over the precordium, commonly seen in right ventricular dilatation, are confused with those appearing in pericardial adhesions.

The upper abdomen usually protrudes owing to the massive enlargement of the liver. Sometimes the contrast between the large pear-shaped abdomen and the small extremities is striking. In other patients, edema of the lower extremities is a prominent sign although this is less regular than ascites.

Highly suggestive in some patients with fixation of the lower sternum is the reversal of chest movements during respiration when the patient is viewed in profile (Wenckebach). Sometimes the position of the lower sternum in expiration closely approximates the position normally seen in inspiration.

Palpation. This method of examination does not afford much assistance. Rarely, compression of the pulmonary artery by a scar causes a supravalvular stenosis and a systolic thrill is palpable; occasionally tracheal tug is present.

Pulsus Paradoxus. Usually the pulse is regular; rarely, atrial fibrillation complicates pericardial adhesions.

There is a periodic inspiratory reduction in the size of the regular pulse called pulsus paradoxus. This finding is easily demonstrated with the auscultatory measurement of the blood pressure since the systolic pressure level changes in different phases of respiration. Pulsus paradoxus may be noted in a great variety of illnesses and even in healthy people. When the clavicle is thrust back, the pulse may disappear in the radial artery because of the compression of the subclavian artery between the clavicle and thoracic cage. This is called paradoxical pulse of extrathoracic origin. A physiologic phenomenon is the so-called dynamic pulsus paradoxus, in which the pulse becomes smaller in inspiration and very large at the beginning of expiration because of the retention of large quantities of blood in the lung during inspiration. With the beginning of expiration this blood is expelled into the left heart. In the paradoxical pulse associated with pericardial adhesions, the pulse is smallest in deep inspiration and largest in the pause at the end of expiration, because with inspiration fibrotic bands compress the aorta more and more while with expiration this compression diminishes.

Figure 52 shows a pulse tracing obtained from a patient with pericardial adhesions The pulse becomes smaller in inspiration and the largest pulse waves are visible at the end of expiration

Venous Pressure Blood Pressure The venous pressure is increased to many times the normal value It is continuously high The arterial blood pressure tends to be lower than normal and the pulse small In an attempt to maintain a normal minute volume there is usually a slight but definite tachycardia

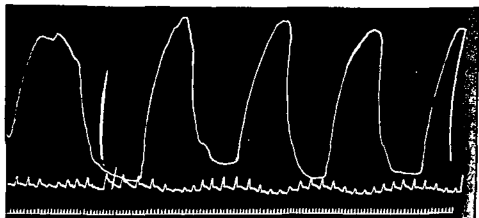


FIG 52 Pulsus paradoxus in a patient with pericardial adhesions

Percussion This may reveal a heart normal in size and shape although some enlargement may be found at necropsy often the heart seems remarkably small

Auscultation Often only pure sounds are found In some cases the heart sounds are dull and split We would consider a duplication of the second heart sound that is frequently heard over the second left interspace as the most common auscultatory finding in patients with pericardial adhe ions Occasionally the first heart sound is duplicated at the apex Protodiastolic gallop rhythm appears Mounsey found an early diastolic sound in 18 of 22 patients with pericardial adhesions It appears on the average 0 1 second after the beginning of the second heart sound The abrupt halting of the filling of the right ventricle is apparently responsible

In pleuropericardial adhe ions systolic clicks appear (systolic gallop rhythm) probably caused by systolic tension of adhesive bands

Other Signs Palpation of the abdomen reveals the enormous enlargement of the liver Congestive cirrhosis of the liver frequently develops After paracente is the spleen may also be felt Despite the venous engorgement a caput medusa is remarkably rare When large amounts of fibrin are deposited on the surface of the liver friction fremitus is occasionally noted

Often the legs are edematous this finding may recede after abdominal paracentesis but once it has developed it rarely vanishes entirely Clubbed fingers represent an interesting and not too unusual finding

Roentgen Examination and Electrocardiogram

Roentgen examination often reveals normal findings in a simple obliteration of the pericardial cavity It may add evidence of pleural or pericardial adhesions (tenting at the cardiac borders) and show indications of calcification in the form of radiopaque bands Frequently the cardiac borders are indistinct Fluoroscopy often furnishes suggestive evidence of diminished movement of the cardiac borders and absence of lateral displacement of the heart on change of posture

The electrocardiogram often shows slurring and notching of the QRS complexes and low voltage

Differential Diagnosis

All the symptoms and signs mentioned above may be modified when other conditions are present Thus a left pleural effusion is frequent and polyserositis is not unusual Right pleural effusion is often missing due to pleural adhesions Moreover in accretio cordis the size and shape of the heart may be altered by the presence of some valvular disorder As a rule however the absence of any right sided cardiac enlargement stands in sharp contrast to the massive liver and great venous stasis When the pulmonary artery dilates as the result of increased pressure in the lesser circulation the heart becomes mitralized the adhesions and obstruction to respiration are responsible Slight rotation of the heart may also cause the cardiac waist to disappear These signs in addition to the small pulse and the splitting of the first sound with duplication of the second sound may suggest the erroneous diagnosis of a silent mitral stenosis Such a mistake is understandable since a duplication of the first sound is often audible at the apex whereas the duplication of the second sound is heard best in the second left interspace Sometimes the protodiastolic accessory heart sound is associated with a palpable shock While this is not peculiar to pericardial adhesions it may be unusually distinct when they are present

Course

Patients may be classified into silent types the stationary forms and the slowly progressive variety The first may be asymptomatic throughout life In others a fairly satisfactory equilibrium can be maintained for years particularly when collaterals form and the constriction of the superior or inferior vena cava is relatively slight In the third group chronic passive congestion of the liver sooner or later leads to congestive cirrhosis

Treatment

Since powerful mercurial diuretics and ammonium chloride were introduced a very tolerable state can often be maintained for years Paracentesis for ascites can be almost entirely avoided if the injections are properly spaced formerly the loss of protein as the result of a rapid succession of abdominal tappings soon

created hypoproteinemia and caused marked cachexia Treatment of the heart itself usually can be omitted because this organ is not primarily affected as a matter of fact it is not decompensated at all for the disease is extracardiac

Until recently cardiolysis the resection of the third fourth and fifth ribs in the region of the heart was the method of choice for surgical cases Despite the doubt cast upon the rationale of the procedure the liberation of the heart from cicatrices which angulate or rotate the viscus is often followed by considerable improvement The operation does not seem to help at all in the constrictive variety For this purpose a cautious decortication may be attempted in properly selected cases Sometimes the results are miraculous and health is restored Unfortunately the mortality rate is high (about 20 per cent) This holds particularly for patients with active tuberculosis for the underlying disease is often aggravated by the operation This will certainly change with the wider use of streptomycin and isoniazid Naturally surgical intervention is doomed to fail if the great veins are clamped by adhesions since the constricting cords cannot be severed owing to the danger of incising the vessels

CALCIFICATION OF THE PERICARDIUM

This condition is clinically unimportant since it is not responsible for any complaint or any cardiac failure which may coexist Nevertheless its occurrence possesses some importance because calcification of the pericardium may be regarded as unequivocal evidence of the presence of adhesions

Pericardial calcification formerly considered very uncommon is not an especially rare event and may be expected in approximately 10 per cent of all necropsies for pericarditis (Smith and Willius) It is encountered at all ages and in both sexes It has been reported as early as the sixth year of life and as late as the ninetieth year Males are more often affected than females In 125 cases compiled by one of us 84 were discovered between the ages of 30 and 70

Pericardial calcifications must be differentiated from calcified valves myocardium or mural thrombi (Klason)

Symptoms and Signs A previous history of pericarditis is rarely obtained The most remarkable feature about pericardial calcification is the extent of the deposit and its completely asymptomatic nature If symptoms or signs occur they are not pathognomonic

Pericardial calcification in our experience is most often discovered accidentally usually it is found by chance during a gastrointestinal x ray series since it is seen much more often during fluoroscopy than in the x ray plate of the chest

The calcific deposit assumes a variety of shapes in x ray pictures When typical a crescentic or sickle shaped shadow is observed when the chest is inspected in several planes Frequently the calcium deposit is diffuse and merely confers increased density upon the cardiac shadow Often it is hidden in the abdominal shadow and escapes detection even when a careful search for it is conducted The deposits are found most often along the coronary sulci

Treatment No therapy is required However the presence of a calcium deposit may influence the surgical approach for the relief of cardiac constriction It is extremely dangerous and rather unnecessary to remove calcium plaques over the thin walled atria Moreover plaques over the ventricles sometimes extend into the muscle and an attempt to remove them has been followed by myocardial laceration and cardiac perforation The same situation holds true for plaques surrounding the inferior vena cava lacerations of this vessel during an attempt to remove an encircling plaque has been in our experience an important factor in the unnecessary mortality during pericardiectomy

MALFORMATIONS OF THE PERICARDIUM

Malformations of the pericardium observed in connection with ectopia cordis and monsters have no clinical interest However there are a series of pericardial defects ranging from complete absence of the pericardium to minor lateral foramina near the root of the left lung which are compatible with life

In most cases the defect produces no symptoms and has no effect upon the duration of life Antemortem discovery may be made in the course of an operation for diaphragmatic hernia The diagnostic criteria consist of a greatly increased motility of the heart cardiac hypertrophy without ascertainable cause and displacement of the heart to the left

Among 46 cases compiled by one of us 20 per cent died from pneumonia and 27 per cent had a fresh pleuropericarditis at necropsy Perhaps the absence of a pericardium renders the heart more susceptible to the extension of an infection from neighboring structures

No treatment is required

Diverticulum A true diverticulum of the pericardium is rare Usually it is situated on the right side It depends upon the protrusion of the serosa through a small defect in the tunica fibrosa False diverticula are usually associated with loculated pericardial effusions The diagnosis depends upon the discovery of a round or polygonal shadow of the same density as that of the heart more or less pulsating and resting with a broad base on the right anterior cardiac shadow This unchanging radiologic shadow is unaccompanied by symptoms manifestations if present remain stationary The negative previous history and the latent evolution distinguish the lesion from mediastinal pleurisy and encapsulated effusions of the right interlobar fissure The absence of symptoms tends to exclude aneurysm while the negative findings in adjacent organs eliminate an extension from a bronchogenic carcinoma or some other pulmonary lesion

TUMORS OF THE PERICARDIUM AND HEART

Since tumors of the pericardium and heart often present similar symptoms and signs they may be discussed together at this point Primary tumors of these structures are exceedingly rare but secondary invasion is relatively common Usually both types escape detection even when a careful search is made

Pathology The most common tumor of the heart is myxoma There is some evidence to suggest that many such tumors are actually organized atrial thrombi According to some investigators however we are dealing with a true new growth The diagnosis is possible as Mahaim points out when peripheral emboli of fragments of the myxoma are recognized histologically Typical pictures may be obtained by means of angiocardiography Surgical cure is possible

A large tumor mass in the left atrium will cause symptoms and signs of congestion in the lesser circuit The usual clinical diagnosis as a matter of fact is that of a mitral stenosis particularly when the myxoma (or fibromyxoma) develops on a valve leaflet The mass may even act as a ball thrombus

Lipoma of the heart is rare and there is an intrathoracic lipoma that develops in the anterior mediastinum and projects toward the base of the neck this lipoma is often confused with a cardiac tumor The precise nature of cardiac rhabdomyoma is disputed Bronchogenic carcinoma occasionally invades the heart and may even cause the syndrome of coronary artery occlusion

The most frequent new growth of the pericardium is sarcoma a mixed cell tumor with round and spindle cells predominating Endothelioma is the second most common primary pericardial tumor

Lymburner claims that primary tumors of the heart are found in 0 05 per cent of autopsies Much more common are metastatic tumors from carcinoma of the bronchi stomach prostate breast and esophagus A third group is created by continuous growth of a bronchogenic or esophageal carcinoma into the heart

Symptoms In a fairly large percentage of the cases the symptoms are not suggestive of tumor and are referred to the heart The signs depend upon the size and location of the mass which may produce mediastinal pressure In a subgroup of this type there are terminal symptoms of cardiac embarrassment with acute decompensation ascites rapidly enlarging heart serosanguinous pericardial extravasate and cardiac irregularity Intractable congestive heart failure characterizes the course in many patients causing the erroneous diagnosis of chronic myocardial disease to be made frequently in this group Congestive failure involves the major or lesser circulations Sudden unexpected death is not rare in cases of tumors of the right heart and is explained by a variety of mechanisms any of which may operate in individual cases Metastatic cardiac tumor may occasionally simulate subacute bacterial endocarditis when there are vague cardiac findings and when metastases in the liver and other organs are associated with irregular fever

The early emphasis on the great frequency of heart block in cardiac tumor is due to the rather frequent association of heart block with rhabdomyoma In another subgroup the patient presents a localizing symptom such as pseudo thrombosis of the superior vena cava or compression of a large vessel Constant displacement of the RS T segment in a patient with metastatic tumor of the heart has been described (Rosenbaum et al) Metastatic cardiac tumor is a diagnostic possibility when dyspnea and edema are out of proportion to the known pulmonary metastasis Other patients present evidence of cardiac dysfunction

that cannot be explained Finally a cardiac tumor and particularly a pericardial new growth may present themselves under the guise of a recurrent accumulation of hemorrhagic pericardial or pleural fluid This symptom is not as common as many observers have inferred The discovery of a blood stained pericardial fluid which is not readily explained by some other process has some diagnostic value In most cases neoplastic cells are not demonstrable in the fluid but an increasing number of positive cases are being reported

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Chapter 15

Congenital Cardiovascular Defects

General Remarks

Our knowledge about the congenital heart lesions has increased enormously in the last few years. With the widespread use of angiocardiography and cardiac catheterization, the observation of a large number of patients during cardiac surgery, and the greater opportunity for postmortem examinations, it has been shown that the clinical diagnosis of congenital heart lesions is possible in most instances. The problem is similar to the one that existed more than 30 years ago concerning coronary thrombosis and myocardial infarction. With the discovery of the electrocardiographic signs of that disease, the diagnosis was made more often with simple clinical methods, and today electrocardiography serves in many patients merely to confirm the diagnosis. Similarly, at present cardiac catheterization and angiocardiography are necessary only in a minority of cases unless surgery is contemplated; in most instances the diagnosis is made on physical examination and evaluation of roentgen findings and electrocardiography.

On the following pages only those congenital heart diseases that are seen in patients over 14 years of age will be discussed.

Cardiac Catheterization and Angiocardiography

Cardiac catheterization was discovered by Forssman and used by him and other physicians for clinical research. Such strong opposition arose to the method, however, that it was soon abandoned. It was Forssman himself who introduced uroselectan into the heart with the aid of a catheter, while O. Klein established measurement of the cardiac output by means of right heart catheterization according to the Fick principle. This method became widely accepted and employed only after the publication of the studies of Cournand and his co-workers.

Catheterization enables one to measure the pressure in the right atrium and ventricle as well as in the pulmonary artery.

Normally the pressure in the right atrium varies from minus 4 to plus 4 mm Hg. Average pressures in the right ventricle are 18–25/0 and in the pulmonary artery 25/8 mm Hg. Catheterization also enables us to analyze the oxygen saturation in these parts of the heart and the venae cavae and to introduce opacifying compounds directly into the heart if necessary. The blood flow can

be calculated by using the Fick principle Impacting a catheter in a pulmonary arteriole permits the pressure in the pulmonary capillaries to be measured and that in the left atrium to be calculated In rare cases of septal defects the catheter will be found in the left heart proving by its mere presence the diagnosis of an abnormal direct communication

It is evident that an increased oxygen saturation in the right atrium if compared to the vena cava superior or inferior speaks in favor of an atrial septal defect while an increased saturation in the right ventricle as compared to the other areas will prove the existence of a ventricular septal defect Catheterization is rarely necessary for the diagnosis of a Fallot syndrome or a patent ductus arteriosus

The dangers should not be minimized Trauma to the veins or the endocardium may result in a thrombus and lethal pulmonary embolism air embolism has been observed The mechanical stimulus of the catheter in the ventricle can cause not only arrhythmias but also on rare occasions ventricular fibrillation and death The mortality is about 4 per thousand

For the diagnosis of aortic coarctation translumbar aortography has been performed or a catheter has been inserted into an ulnar or brachial artery and pushed up in the aorta Damage of the aortic wall or the aortic valve has been described so that this method should be used only rarely For the diagnosis of an aortic or mitral valvular lesion evaluation of the degree of the individual lesions or evaluation of the degree of left ventricular failure from the diastolic left ventricular pressure catheterization of the left heart has been developed Transbronchial or percutaneous transthoracic puncture of the left atrium is performed

Angiocardiography causes death in about 2 per cent of the cases and should be performed only to clarify the picture before surgery A second injection is particularly dangerous because of hypersensitivity and the method is especially risky in very cyanotic children Sensitivity tests are of little value A vein is usually exposed and the agent injected in an amount of 50 ml within one or two seconds Local venous thrombosis often occurs

Details of the value of these methods will be discussed in pertinent sections It is most useful in cyanotic lesions with right to left shunt

Other Diagnostic Factors

Circulation Time The determination of the circulation time aids in the diagnosis of some congenital abnormalities namely those with a right to left shunt which permits the injected substance to reach peripheral arteries more quickly than normal The arm to tongue time and the arm to lung time are determined a shunt of appreciable dimensions is assumed to exist when both agree within 2 seconds An arm to tongue time of less than 10 seconds speak in favor of a venous arterial shunt

Clubbing of the fingers or toes can be familial In this case it is often asymmetrical It is unilateral or even limited to one finger if it is caused by a local

disturbance of circulation In hypertrophic osteoarthropathy in congenital heart lesions the proximal bones are involved in addition to the phalanges Hyperplasia and hypertrophy appear in the soft tissues the bones become osteoporotic and patients experience pain More than 60 years ago Bamberger considered an increased peripheral blood flow as an etiologic factor but still little is known about the mechanism

Pulmonary Plethora and Ischemia In addition to the division of congenital heart lesions into cyanotic and acyanotic types they are also classified into those with pulmonary plethora (patent ductus arteriosus transposition atrial and ventricular septal defects) and pulmonary ischemia (pulmonary stenosis Fallot s tetralogy tricuspid atresia)

Cyanosis The depth of cyanosis depends not only upon the degree of the venous arterial shunt but al o on the secondary pulmonary vascular changes and polycythemia

One should be careful not to confuse congenital heart lesions with congenital and acquired forms of methemoglobinemia the latter has been observed in children on a formula made with well water containing a high content of nitrites

Severe cyanosis is seen in transposition of the great vessels actually in children with large hearts and severe cyano is one should consider this ab normality first Here the aorta carries unoxygenated blood and the pulmonary artery returns fully oxygenated blood to the lungs Life is possible only if septal defects or a patent ductus arteriosus coexi t Severe cyanosis also occurs in tricuspid atresia when all blood is shunted from the right into the left atrium It is also seen in Eisenmenger s complex in pulmonary atresia with a riding aorta and septal defect and occasionally in pulmonary arteriovenous fistulas

Slight cyanosis occurs in pulmonary stenosis Fallot s tetralogy some atrial septal defects and in truncus aortae communis In Eisenmenger s syndrome cyanosis appears late (at puberty) In atrial septal defects cyanosis may appear in infants and children during crying and coughing when the shunt reverses due to the changes in pressure and the flow goes from right to left

Anoxia Attacks of sudden anoxia are not rare particularly in Fallot s syndrome Morphine (0 5—1 0 mg per 10 pounds of body weight) is useful

Cardiac Pain Cardiac pain is occasionally present owing to hypoxia of the heart muscle It was found in 4 8 per cent of 480 patients with congenital heart disease (Stuckey)

Squatting Taussig pointed out that some children with congenital heart disease e g those with Fallot s tetralogy assume a squatting position The reason is unknown A compression of the abdomen whereby a larger amount of blood is forced back to the heart has been considered a factor

Marfan s Syndrome This abnormality is often found in patients with heart disease One of the most interesting changes is arachnodactyly or spider fingers Patients with this syndrome are often thin and slender with under developed muscles and hyperflexible joints They may have a high arched or cleft palate a pigeon or funnel chest prominent supraorbital ridges large ear

lobes sunken eyes with subluxation of the lens and nystagmus the metacarpal metatarsal and phalangeal bones are abnormally long and the distal parts of the fingers attenuated deformities of the feet and kyphoscoliosis are common Patients look older than they actually are and often have a sad melancholic expression All these signs are rarely present simultaneously in a given patient and there are many abortive cases The syndrome occurs in families In one instance four siblings were affected It has been called dystrophia mesodermalis congenita and is attributed to a general mesenchymal malformation

Congenital abnormalities of the heart or aorta are found in one third to one half of these patients The heart usually shows septal defects while congenital aneurysmal dilatations occur of the aorta or pulmonary artery dissecting aneurysms occur in the aorta the observation of aortic regurgitation has been mentioned in another chapter

Other Syndromes It is estimated that 25 to 50 per cent of the cases of mongolism harbor a congenital heart lesion Of great interest is Kartagener s syndrome which consists of chronic sinusitis bronchiectasis and situs inversus totalis

Etiology

The cause of congenital heart lesions is not entirely clear In the past lues was often suspected as was consanguinity of the parents alcoholism conception in an elderly mother (exhaustion products) or many conceptions at short intervals There is a definite familial tendency

A very important recent discovery throws new light on the problem It has been shown that congenital cataract congenital deafness hare lips cleft palate microcephaly and congenital heart lesions appear in a high percentage of children borne by mothers who had rubella (German measles) in the first three months of pregnancy This early date is important because in an embryo of seven weeks the heart already possesses its permanent shape and the septa are formed Of interest is the observation that the above named abnormalities were observed in mothers who had rubella before conception other observations showed the occurrence of these congenital abnormalities when the mothers had the disease in the eighth or even the ninth month of pregnancy A similar syndrome has been observed following infectious mononucleosis According to some investigators this of fection occurs in 90 per cent of cases with German measles while others found it in only 27 per cent It is assumed that the virus passes through the placenta into the fetus the variation in the incidence is understandable since the diagnosis of congenital heart disease is made by some authors solely on the basis of a systolic murmur whereas others use more rigid criteria Possibly as many as 5 per cent of congenital heart lesions may be attributed to rubella or a similar infection but these diseases may be so mild that they can easily be overlooked by both the physician and the patient

Because of the high incidence of eye ear and heart abnormalities following rubella in the early months of pregnancy the interruption of the pregnancy in such cases has been considered An evaluation of this problem has been written

by Wessell While some authors are in favor of an interruption others are not entirely convinced of its necessity

In this connection the experiments of Gilman Gilbert and Spence are highly revealing They injected pregnant female rats with trypan blue which is bound to proteins and alters the plasma proteins In 19 2 per cent of the litter gross congenital abnormalities were found If rats were given a diet deficient in pteroylglutamic acid during the gestation period fetuses showed ventricular septal defects persistent ductus arteriosus and other anomalies (Baird et al) Congenital cardiac anomalies can be seen in rats and mice after x ray irradiation or as a consequence of anoxia

The exposure to radiation either in the form of fluoroscopy or radiography should be limited during the early months of pregnancy X ray radiation anoxia insulin injections and vitamin A deficiency in rats and other experimental animals may lead to congenital heart lesions in the offspring

Secondary Phenomena In patients with congenital heart lesions with and without cyanosis mental retardation is common Growth is also slow Nosebleed and hemoptysis occur and complications such as arterial thrombosis due to polycythemia are observed Marked atherosclerosis develops in the arteries of the lesser circuit Cerebral abscesses either solitary or multiple are not rare particularly when blood reaches the cerebrum without filtration by the lung (they should be treated surgically and with antibiotics)

Further Remarks Owing to the appearance of an abnormality in a developing organ in which the evolution of one part often depends to a great extent upon the proper unfolding of another solitary lesions are less common than combined ones

In embryonic development the heart gradually passes through different stages that closely resemble those of the fish amphibian and bird heart Phylo genesis is repeated in ontogenesis Since the development may stop in any stage the heart (or great vessels) in man occasionally resembles the structures found in lower animals

Congenital heart lesions are not especially uncommon for they are found in more than 1 per cent of routine necropsies Many lesions such as persistent right aortic arch coarctation of the aorta or small defects of the ventricular septum may be recognized late in life and are found accidentally since the patient may feel perfectly well

Owing to the early appearance of some of the changes and the slow development of others and due to the activity of compensatory mechanisms these patients often have surprisingly few complaints This occurs despite the fact that examination of arterial blood reveals a status which would hardly be compatible with life had it developed acutely

Congenital heart lesions have been classified into the cyanotic and acyanotic group Acyanotic lesions are exemplified by coarctation of the aorta most cases of patent ductus arteriosus ventricular and atrial septal defects subaortic stenosis and anomalies of the aortic arch In a large percentage of cases cyanosis is a

late event and often is transient (cyanose tardive late cyanosis) This variety is found in atrial or ventricular septal defects or with patent ductus arteriosus Blood always flows from areas with high pressure to areas with low pressure in the cases mentioned above this is usually from the arterial to the venous side cyanosis is therefore absent If however during decompensation or because of arterial spasm in the lesser circuit pressure increases the flow is from the right atrium right ventricle or pulmonary artery to the corresponding structure in the left heart venous blood will then intermix with arterial blood and cyanosis appears

One of the best known and most common complications of a cardiac malformation is subacute bacterial endocarditis noted in 16 5—19 6 per cent of the cases It seems more frequent in the acyanotic group and is especially common in interventricular septal defects in patent ductus arteriosus and in some asymptomatic lesions like bicuspid aortic valves

The mechanical strain (jet action) at an abnormal location of the endocardium or endothelium of blood vessels is the main reason for infection with streptococcus viridans

So called congenital idiopathic hypertrophy of the heart about which a great deal was formerly written is scarcely diagnosed at present Most cases are now explained by previous myocarditis hypertension in the lesser circuit von Giercke s disease avitaminosis etc Myocardial fibrosis is a common postmortem finding

The electrocardiogram in patients with congenital heart disease rarely has decisive value for the diagnosis In many lesions with augmented strain on the right heart right axis deviation is found In atrial septal defects widening slurring and notching of the QRS complex is very common Sometimes the P waves are higher than normal this happens chiefly in pulmonary stenosis with and without a septal defect

If the congenital heart lesion produces no murmurs differentiation from a cor pulmonale due to pulmonary pathology may be a difficult problem at times

Congenital abnormalities of the coronary arteries will be considered in the next chapter

ATRIAL SEPTAL DEFECTS

Embryology The primitive heart is a simple tube lined with endocardium folds develop in this tube demarcating the various sections Accordingly the primitive atrium is a single structure Early in embryonic life a sickle like fold develops from the upper posterior aspect and passes downward toward the atrioventricular border At the lower border of this fold an opening (the foramen primum) persists temporarily since the septum does not extend sufficiently far In the meantime a gap forms in the primitive atrial septum near its point of origin (the foramen ovale primum) A second fold appears near the original septum and develops more or less as a ring It embraces an oval opening (foramen ovale secundum foramen ovale) Ordinarily the first and second septa fuse and

the foramen ovale secundum closes soon after birth Within the first twelve weeks of life the foramen ovale is closed in 81 per cent of children

The foramen primum type of lesion is often combined with valvular deformities of the mitral valve sometimes a common atrioventricular canal exists The clinical differentiation between the two types is very difficult

Pathology Interatrial communications may be mere slits (probe patency) in the region of the foramen ovale (persistent foramen ovale) This is a very common event and is found in approximately 20 per cent of all necropsies The opening may be 6 to 8 mm in diameter Under ordinary conditions it has no great importance but it may explain some disturbances noted in advanced stages of mitral stenosis or emphysema if pressure in the right atrium rises unduly the foramen is normally closed by a fold This is pushed open by high pressure in the right atrium and marked cyanosis appears due to the right to left shunt

Interatrial communications may also result from a failure of the septum primum to descend normally or because of abnormal regression of the septum primum In these cases the mitral and tricuspid valves often show abnormalities Atrial septal defects are also caused by agenesis of some parts of the septa In this type of septal defect the communication between the two atria may be large In the extreme cases the atrial septum is absent and one speaks of a cor triloculare biventriculare a three chambered heart with one atrium and two ventricles

Incidence Atrial septal defect is one of the most common heart lesions in adults and according to statistics it comprises 7—25 per cent of cardiac malformations In the past it has been frequently overlooked its symptoms being considered clinically the result of a mitral lesion The malformation is more common in women than in men

Pathologic Physiology The flow through the shunt from left to right has been found in some patients to vary from 1 4 to 16 liters per minute The output of the right ventricle per minute may be four times larger than that of the left ventricle In spite of the marked increase of flow through the lesser circuit pressure there need not increase With larger defects there is also at the same time reversed shunt from right to left which causes a fall in the oxygen saturation in the aorta Secondary vascular changes (spasms and later sclerosis) in the lungs increase the pulmonary arterial pressure The greater pressure in the left atrium as compared to the right one is explained by some authors by the greater resistance the thick walled left ventricle offers to the inflow of blood as compared to the thin walled right ventricle

Symptoms The disturbance may exist for many years without symptoms Often evidence of decompensation appears in patients beyond the age of 30 However patients are known who have been active much longer One of our patients is now 72 years old and still active

The signs are usually those of right heart failure i e edema and hepatic enlargement Dyspnea and palpitation occur much earlier but they are moderate Precordial pain may appear

Signs Cyanosis is absent for a long time appearing only when pressure rises in the right atrium and causes the shunt of venous blood in appreciable amounts into the arterial system Cyanosis may also be noted as an intermittent phenomenon for example during bronchopneumonia coughing spells in the newborn or infants or physical exertion with increase of pressure in the right atrium Only in the final stage is cyanosis continuous and deep



FIG 53 Characteristic roentgenogram of a woman with an atrial septal defect

Examination reveals a small peripheral pulse and a systolic or sometimes a diastolic thrill over the pulmonary artery The heart seems mitralized on percussion and there is evidence of dilatation to the right and to a lesser extent to the left A harsh systolic and sometimes a blowing soft diastolic murmur are audible over the pulmonary area The systolic murmur may be soft and may be confused with an insignificant (functional) murmur if the defect is small It appears sometimes after years since following birth the pressure in both atria may be equal The first apical sound is loud The systolic murmur is explained by eddies created in the dilated pulmonary artery with increased flow of blood (mechanism of relative pulmonary stenosis) The diastolic murmur over the same artery was observed in 10 of 53 cases (Bedford et al) whirling of blood caused by the abnormally dilated conus or in the dilated right atrium is assumed to be provocative A relative pulmonary insufficiency is often present (Graham Steell murmur) On the other hand occasionally no murmurs may be heard Furthermore it is characteristic for this lesion to have the murmurs come and go with changes of posture

The second pulmonic sound is accentuated and often split

Roentgen Examination The radiologic signs usually permit the diagnosis The heart is enlarged The prominent arc of the pulmonary artery is typical The

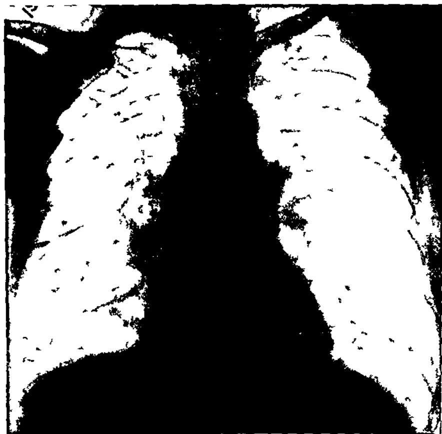


FIG 54 Marked widening of the pulmonary arteries in a patient with an atrial septal defect simulating neoplastic masses in the hilar regions

descent of the main branch of the right pulmonary artery is clearly visible in the right lung field Even its bifurcation into individual branches may be seen The lungs are not congested as is ordinarily seen in a mitral stenosis The left atrium and the aortic knob seem to be small while the right heart is enlarged The pulsations of the pulmonary arteries are accentuated and a real hilar dance occurs The right atrial appendix may be visible on top of the right atrium (Kjellberg et al)

Figure 53 was obtained from a 61 year old woman who complained of shortness of breath on exertion for the past 18 years There was no history of rheumatic fever Figure 53 shows the prominent conus of the pulmonary artery and the large right hilus the main branch of the right pulmonary artery is visible The

heart is enlarged to the right and to the left due to right ventricular dilatation On fluoroscopy hilar dance was pronounced The lung fields are clear The left atrium was enlarged There was no evidence of a mitral lesion

A rough systolic murmur was heard over the pulmonary artery

In some cases a coeur en sabot (Vaquez and Bordet) is found The dilatation of the right ventricle is so marked that this structure forms all but the middle section of the left cardiac border In the border between the right and left ventricle a small sharp edge is visible that gives the impression of a wooden shoe

The shadows of the unusually widened pulmonary artery have been confused with masses caused by bronchogenic carcinoma or Hodgkin s disease (figure 54)

In many cases other congenital abnormalities coexist and may render the diagnosis more difficult The differentiation from some other lesions causing prominence of the pulmonic arc such as ventricular septal defects patent ductus arteriosus or pulmonary stenosis is usually possible but may be difficult at times The features which permit the diagnosis of a persistent common atrioventricular canal in patients with an atrial septal defect are discussed by Wakai et al

Electrocardiography In addition to right ventricular hypertrophy the electrocardiogram shows intraventricular conduction disturbances with slurring and notching of the QPS complexes so that sometimes the picture of right bundle branch block is present Often the P waves are large and rarely the P R interval is prolonged

Catheterization This method permits the diagnosis immediately if the catheter passes through the septal defect and reaches the left atrium and ventricle The oxygen saturation in the right atrium is characteristically greater than in the venae cavae as it is in anomalous pulmonary veins or in ventricular septal defect with tricuspid insufficiency A difference of at least 2 volumes per cent is decisive Slight differences are seen normally This finding is missed when the shunt is reversed from right to left the shunt is often mixed as was discussed above this happens particularly when emphysema or secondary pulmonary vascular changes raise the pressure in the right atrium

Angiocardiography This procedure shows a large right atrium that remains opacified abnormally long because of the shunting of left atrial blood back into it (recirculation) In the left oblique position the shunt may be visible If the above named complications cause a shunt from right to left angiocardiography shows immediate filling of the left atrium

Differential Diagnosis The differentiation of the lesion from an anomalous venous return ventricular septal defect and patent ductus arteriosus is possible in most cases because of the syndromes which will be discussed in the following pages occasionally however the diagnosis is difficult when based on clinical findings alone In pulmonary stenosis the lungs are oligemic Primary pulmonary hypertension is easily confused with this lesion as is a silent isolated mitral stenosis High ventricular septal defect with a communication between the left ventricle and right atrium may be confused with an atrial septal defect on the

basis of catheterization data surgery in such cases may have a fatal outcome (Stahlman et al)

Lutembacher s Syndrome A well known complication is a rheumatic mitral stenosis The combination of an atrial septal defect and mitral stenosis is known as the Lutembacher syndrome In one series of 60 cases of atrial septal defects mitral stenosis was found clinically 12 times Some observers find the combination much more rare and we agree with them Apical diastolic murmurs can be heard in the absence of mitral stenosis when large quantities of blood rush into the ventricle

The diagnosis of Lutembacher s syndrome is easy when the typical prolonged diastolic apical murmurs of mitral stenosis are present It may be impossible in the absence of the murmurs since the symptoms and signs are the same as in an uncomplicated atrial septal defect The left atrium usually does not enlarge presumably owing to the fact that the communication between the atria prevents great congestion in the left atrium and the rise of pressure is transmitted early to the right atrium

It is astonishing that the changes in the heart and therefore in the dynamics are the same irrespective of whether the septal defect is complicated by a mitral stenosis or not It has been pointed out that the flow of blood from the left into the right atrium in atrial septal defects may result from the fact that the left atrium lies cephalad to the right and the septal defect lies in a horizontal plane Thus the arteriovenous shunt may be due simply to gravitational flow

Complications Paradoxical embolism occurs in atrial septal defects and in open foramen ovale Atrial septal defects are the only congenital heart lesions in which atrial fibrillation is common Subacute bacterial endocarditis on the other hand is rare

Prognosis Most of those affected succumb before the fiftieth year Even when a mitral stenosis is present patients may occasionally reach an old age as the case of the oft quoted 74 year old woman shows she had 11 pregnancies and 3 abortions (Firket quoted by Abbott) Pregnancies usually are tolerated well

Surgery Several types of operations have been recommended A plastic button or simple suture has been used (Cross Hufnagel) and many patients have recovered following such intervention Operation is indicated when evidence appears that the load for the right heart is too great A high defect (also called patent ostium secundum) is relatively easily closed Low defects near the valves are closed with difficulty Valvular anomalies are common in such patients The heart is larger and symptoms begin earlier

Bailey et al treated atrial septal defects by atrioseptopexy Ninety per cent of the patients survived the operation with marked clinical improvement when a patent ostium secundum deformity existed However 11 of 16 patients succumbed to surgical correction of an ostium primum One does not operate when a right to left shunt exists

ANOMALOUS PULMONARY VEIN DRAINAGE

This anomaly does not seem to be rare and has become better known only after the wider use of cardiac catheterization The clinical picture is similar to that seen in atrial septal defect In this anomaly one or more of the main pulmonary veins do not empty into the left atrium but into the azygos vein the superior or inferior vena cava or even the coronary sinus vein thus connecting back into the right atrium Often the veins drain into a persistent left vena cava superior If all pulmonary veins drain abnormally a septal defect must exist to be compatible with life and even then these individuals usually die in infancy In the partial form of the anomaly an atrial septal defect may also coexist When less than 50 per cent of the pulmonary venous blood drains into the right atrium cyanosis is absent and patients have been known to reach the age of 80 or more

There are no characteristic findings on physical examination A systolic and rarely also a diastolic murmur may be heard over the base of the heart The second pulmonic sound may be split There is right ventricular hypertrophy and a widened pulmonary artery is seen similar to that observed in atrial septal defects The abnormal hemodynamic mechanism is the same The electrocardiogram shows the same changes as seen in atrial septal defect The differential diagnosis is impossible on clinical grounds but roentgenologic examination is helpful Often one sees ovoid masses in the lung running parallel to the cardiac shadow particularly when a pulmonary vein flows into the vena cava inferior The upper mediastinum shows bulging Snellen and his co workers described a figure of eight mass on the upper cardiac mediastinal area Tomography permits one to follow these abnormal veins and to see their connections which were mentioned above

Often the cardiac catheter is pushed into these abnormal veins and arterialized blood is withdrawn Angiocardiography shows the abnormal veins clearly

Surgical therapy with transplantation of these abnormal veins into the left atrium has been successfully attempted It is a difficult operation If one small vein drains abnormally the portion of the lung from which it comes can be extirpated Even total anomalous pulmonary venous connection has been corrected surgically with success (*Burroughs*)

PATENT INTERVENTRICULAR SEPTUM

Pathology This congenital defect may appear alone or in combination with other lesions In its pure form it is not as common as generally believed

Uncomplicated *small* patent interventricular septum is often called maladie de Roger after one of the first authors to describe it According to other authors the term Roger s disease should be used only in those cases in which the defect is within the muscular septum We do not see any reason why all pure ventricular septal defects should not be called Roger s disease

In lower muscular defects the murmur is in a lower intercostal space However in a majority of cases (90 per cent) the defect is situated at the membranous

septum (undefended space) Therefore it lies just beneath the aortic valves and communicates with the right ventricle behind the septal cusp of the tricuspid valve Its diameter varies from 0 2—3 cm in most cases The defect develops if the bulbar septum fails to descend properly and does not close the foramen interventriculare in the interventricular septum The defect becomes relatively smaller when the heart grows

Often the opening is very small and only permits the passage of a small probe while in other instances it may be wide enough to admit a thumb If the interventricular septum fails to develop a cor triloculare biatriatum results Children with this condition rarely live beyond the age of four years Acquired septal defects are discussed in the chapter on coronary thrombosis

Symptoms Many patients are fully active and free from complaints for many years This happens particularly in those with a small opening when the lesion is often overlooked There are no characteristic symptoms but dyspnea and palpitation may appear in the late stages Fatigue is one of the earliest symptoms

Signs There is no cyanosis for a long time since the blood flows from the left ventricle (with its higher pressure) into the right ventricle In later years complications such as pulmonary emphysema may increase the pressure in the right ventricle so that cyanosis appears at first only on exertion but eventually continuously In large defects the pulmonary resistance is increased very early and a reversed shunt may occur

Physical examination reveals a prolonged systolic thrill over the third or fourth intercostal space to the left of the sternum This is present in only a third of the cases Frequently in the early stages the size of the heart is normal general (right and left ventricular) dilatation may appear later There is no characteristic configuration The pulmonary arc may be prominent and the hilar shadows are increased pulsations of the hilus (hilar dance) may also occur The underdevelopment of the aortic knob may be explained by the fact that much of the output of the left ventricle is lost into the right ventricle As much as 50 per cent of the left ventricular output may be forced into the right ventricle

There is a very loud prolonged harsh rasping systolic murmur with a point of maximum intensity in the third fourth or fifth interspaces to the left of the sternum often it is transmitted to the back This murmur as in other stenotic mechanisms may be louder when the defect is small (figure 55) It may be absent when the same pressures prevail in both ventricles The murmur usually is of steady intensity that is neither crescendo nor decrescendo it may become louder when the patient lies in the left lateral position It may or may not be widely transmitted The second pulmonic sound may be accentuated whereas the second aortic sound is often softer than usual A diastolic apical or pulmonary murmur explained by turbulences and eddies in the left ventricle or pulmonary artery may be heard

Figure 55 shows the stethogram of a child with ventricular septal defect The electrocardiogram is often normal and never characteristic

Patients may reach old age despite the defect Fifty per cent of patients with large septal defects die early in childhood Open heart surgery with extra corporeal circulation now saves many lives

Catheterization and Angiocardiography Cardiac catheterization reveals a high oxygen saturation in the right ventricle this saturation is higher in the upper parts of the right ventricle than in the right atrium Later in the disease if pulmonary resistance and pulmonary pressure rise a right to left shunt occurs and catheterization is of no help It also does not yield sufficiently clear cut data when the opening is small Occasionally the catheter may be pushed into the left ventricle and even into the aorta



FIG 55 Persistent loud murmur filling all systole over the fourth left intercostal space parasternally in an 8 year old child with a ventricular septal defect

Angiocardiography is of no help with small openings With large defects persistent filling or refilling of the right ventricle may be seen An early filling of the left ventricle is only minimal

Differential Diagnosis Differentiation from other congenital cardiac lesions is difficult but is usually possible X ray and fluoroscopy may reveal findings very similar to those in an atrial septal defect (prominent pulmonary arc enlargement of the hilar vessels and hilar dance) The widening of the pulmonary artery and its branches generally is more pronounced in atrial septal defects The systolic murmur in cases of a ventricular septal defect is heard best at a more caudad area it is more prolonged and rougher

If pulmonary pressure rises a relative pulmonary insufficiency may appear The differential diagnosis from pulmonary stenosis may be difficult In this condition the lungs are however oligemic Septal defects can be confused with mitral lesions Differentiation usually is easy by means of the location of the points of maximum intensity and the character of the murmurs

Complications Heart block is an occasional finding This block is usually complete but sometimes only partial Congenital heart block is not necessarily incapacitating and it may occur in the absence of a septal defect Its presence should be expected more constantly than is actually the case since the bundle of His is situated just behind the undefended space Perhaps its rarity may be explained by the fact that the bundle develops before the interventricular septum is

formed Masses of connective tissue often interrupt the path of the atrioventricular conduction system Since cellular infiltrations of the inflammatory type with excessive growth of connective tissue are commonly found, fetal myocarditis has occasionally been assumed However the heart block in patients with ventricular septal defects often is not congenital It develops slowly in the first months or years of life because of thickening and development of fibrotic strands at the edges of the defect

Subacute bacterial endocarditis which develops in more than one third of the patients represents a more serious complication The vegetations are usually situated around the interventricular opening in the right ventricle where the blood pressed through the opening impinges on the wall Therefore pulmonary rather than systemic embolism is more common

Surgery Open cardiac operation with the use of a mechanical pump oxygenator is promising and is preferable to the closed methods Sixteen of 20 patients who were operated on survived and there was only one death among the last 13 of the series (Duane et al) The operation was successful in some patients despite the presence of pulmonary hypertension and the presence of a right to left shunt associated with the left to right shunt

PULMONARY STENOSIS

Pathology Incidence Like congenital aortic stenosis pulmonary stenosis with normal aortic root may involve the infundibulum (conus) the orifice itself or the supravalvular part of the artery The degree of stenosis varies widely The opening of the valves may amount to only a few millimeters Sometimes a dome shaped funnel projects into the pulmonary artery Isolated pulmonary stenosis is usually valvular The main right or left pulmonary artery may be absent with a greatly diminished vascularity of one lung

Pulmonary stenosis is more common than was assumed in the past Often it has not been recognized Not rarely the pulmonary valves are bicuspid

Uncomplicated stenosis of the pulmonary artery is compatible with long life — patients may live to the age of 60 years or more In combination with a ventricular septal defect the lesion is one of the more common congenital anomalies Widening of the area just beneath the stenosis is likewise a common finding as is dilatation of the pulmonary artery beyond an incomplete stenosis In patients with an infundibular stenosis an additional (third) ventricle may seem to be present above the stenosis In instances of a pronounced stenosis of the pulmonary orifice the left ventricle may seem smaller than normal

Symptoms Patients complain of dyspnea fatigue and weakness anginal pain and syncope Often however complaints appear late in life since a slight reduction of the pulmonary circulation will not cause oxygen unsaturation and cyanosis When there is a marked decrease of oxygen saturation squatting occurs

Signs There is evidence of right ventricular hypertrophy on palpation Usually a loud systolic murmur is audible over the pulmonary ostium unless there is a complete atresia It is often accompanied by a thrill The second pul

monic sound may be absent or weak but in some cases particularly in those with a stenosis of the supravalvular type it is loud As in aortic stenosis the systolic murmur may be diamond shaped in the stethogram (figure 56) It is often heard over the back and is often late systolic If there is infundibular stenosis the murmur is heard lower in the third or fourth intercostal space

Occasionally a diastolic murmur is also heard since owing to malformation or a relative type of regurgitation the pulmonic valves are incompetent It is remarkable that this murmur is not heard more regularly with a stenosis of the orifice itself for complete closure of the valves in diastole should be impossible in most cases of stenosis However in a similar way the diastolic murmur of an aortic insufficiency is often absent in an advanced aortic stenosis of rheumatic or arteriosclerotic origin The second pulmonic sound is soft or absent

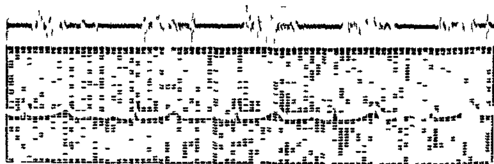


FIG 56 Diamond shaped murmur over the second left intercostal space parasternally in a patient with pulmonary stenosis

X ray examination reveals in patients with an incomplete stenosis of the pulmonary valves a widening of the supravalvular portion of the pulmonary artery that is missing in infundibular stenosis This is explained in a similar way as the widening of the aorta above an aortic stenosis The lungs are oligemic they are however normally vascularized when the stenosis is mild The pulmonary vessels are small

The electrocardiogram shows large P waves and marked right ventricular hypertrophy The T waves are inverted in V1 and V2

Catheterization This shows a typical finding The blood pressure in the right ventricle is high and it suddenly falls when the catheter reaches the pulmonary artery The lowest pressure gradient is 10 to 15 mm Hg The oxygen saturation is the same everywhere Figure 57 shows the sudden fall of pressure when the catheter leaves the right ventricle and reaches the pulmonary artery in a 42 year old man with an asymptomatic pulmonary stenosis

Angiocardiography There is dilatation of the right atrium and ventricle The stenosis is sometimes visible (20 per cent) but the picture is often misleading Not much is gained by this test

Not rarely the high pressure in the right atrium forces the foramen ovale open and marked cyanosis appears suddenly because of a marked right to left shunt. With an open foramen ovale the left atrium fills early. The combination of pulmonary stenosis and open foramen ovale is known as the trilogy of Fallot.

Differential Diagnosis. In pure cases the differentiation from ventricular septal defect is usually easy because in pulmonary stenosis the point of maximum intensity of the systolic murmur is located higher (in the second intercostal space). But sometimes it may be sufficiently low to cause confusion. The loud systolic murmur over the pulmonary area in atrial septal defects combined with

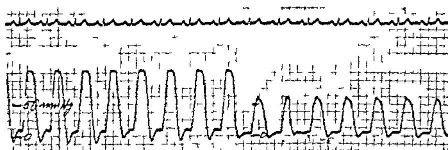


FIG 57. Forty two year old man with pulmonary stenosis (see figure 56). The pressure falls suddenly and appreciably when the catheter is moved from the right ventricle into the pulmonary artery.

a prominent pulmonary arc may also cause mistakes. Under these circumstances the frequent absence of the second pulmonic sound in pulmonary stenosis may help. In pulmonary stenosis the lungs are oligemic. One must also distinguish the lesion from Fallot's tetralogy and Ebstein's disease.

Complications. More often than in any other congenital cardiac disease pulmonary tuberculosis develops due to the abnormal blood supply to the lungs. This is somewhat puzzling since the circulation in the bronchial arteries is not directly reduced. Soulie et al. found that pulmonary tuberculosis was 3 to 4 times as common in patients with diminished blood flow to the lungs as in the general population. Moreover, the evolution of the illness was more acute.

Surgery. Mild stenosis of the pulmonary orifice is not treated surgically. Patients may live to the age of 75 years. In advanced infundibular stenosis resection and dilatation is done (Brock). The operation is best performed when the patient is between the ages of 5 and 12 years. Danger increases in older individuals. The mortality averages about 10 per cent. Campbell and Brock report only 3 deaths in 52 consecutive operations. The vast majority of those who survive showed improvement. The approach in Brock's operation is from the right ventricle.

EISENMENGER'S SYNDROME

In Eisenmenger's triad or complex a large high interventricular septal defect exists causing the aorta to ride over both ventricles There is marked right ventricular hypertrophy and no pulmonary stenosis It has been pointed out recently that separation of a large ventricular septal defect from Eisenmenger's syndrome seems impossible clinically and even morphologically Symptoms and signs are those of a large ventricular septal defect in which a riding aorta must be present

Cyanosis appears late in these patients since the shunt is initially from the left ventricle to the right one However secondary changes in the pulmonary vessels raise the blood pressure in the lesser circuit to a degree that the shunt becomes reversed that is from right to left Sometimes the pressure in the lesser circuit may approximate that in the systemic circulation In these cases the right ventricle may be markedly dilated and signs of right ventricular hypertrophy appear in the electrocardiogram

The roentgenologic signs are those discussed earlier in connection with ventricular septal defects

Catheterization shows an increased pressure in the right ventricle and the pulmonary artery plus the other findings listed in the preceding chapter Roentgen examination and catheterization permit the exclusion of a pulmonary stenosis and therefore a tetralogy of Fallot Angiocardiography shows simultaneous filling of pulmonary artery and aorta It is difficult to differentiate the lesion from essential pulmonary hypertension

There is no surgical therapy

TETRALOGY OF FALLOT

Incidence Pathology This syndrome is found in 75 per cent of adults with congenital heart disease exhibiting clubbing of the fingers and cyanosis Actually it consists of only two defects First there is a pulmonary stenosis which is most often infundibular and in a small minority of the cases valvular Second there is a very large interventricular septal defect which as discussed in the preceding section gives the picture of a riding aorta With the pulmonary stenosis varying from so slight a form that separation from Eisenmenger's triad is impossible to complete atresia and with variations of the size of the ventricular septal defect countless variations are seen Often the foramen ovale is patent

Sometimes a patent ductus arteriosus coexists and makes the diagnosis more difficult Then cyanosis may be absent Large anastomoses exist between the bronchial and pulmonary arteries In cases with pulmonary atresia often the lungs are supplied only by the bronchial arteries A persistent right aortic arch is found in 20 per cent of the cases

Symptoms and Signs Cyanosis appears at birth or after a few years since the pulmonary stenosis raises the pressure in the right ventricle leading to a right to left shunt Squatting is said to be very characteristic (Taussig) Poly

cythemia is marked There is stunting of growth Attacks of unconsciousness occur Brain abscesses are a not infrequent complication

The heart is often a little enlarged and boot shaped (coeur en sabot) and the right ventricle forms a large part of the left cardiac border The lungs are oligemic and the hili are small The concavity in the area of the cardiac waist is conspicuous owing to the absence of a pulmonary conus and a small pulmonary artery The second aortic sound may be loud over the pulmonary area The second sound is not split A systolic murmur and thrill may be found over the base of the heart Often these are absent since the pulmonary orifice is atretic and the riding aorta with a large ventricular septal defect does not cause murmurs The aortic arch is often on the right side this is an important finding if surgery is contemplated The bronchial arteries are enlarged

Laboratory Findings The electrocardiogram shows large P waves in all standard leads particularly in lead II Right axis deviation and signs of right ventricular hypertrophy are common The P waves are very large in V1

With angiocardiography the pulmonary artery and aorta fill simultaneously with the dye The picture of the upper left cardiac border will vary in complete pulmonary atresia and in moderate stenosis In rare cases the degree of pulmonary stenosis can be ascertained In the left oblique position the aorta may be seen originating from the right ventricle

With cardiac catheterization the tip of the catheter may be found in the aorta Pressure in the right ventricle may reach values of 100/5 mm Hg The pressure in the pulmonary artery has been found low in those subjects in whom the catheter can pass the stenosis The catheter may be pushed into the aorta and pressure in the aorta and pulmonary artery may be identical In some cases the localization and the degree of pulmonary stenosis cannot be determined with angiocardiography and catheterization The oxygen saturation of the blood in the right ventricle is identical with or even higher than that of the right atrium

Differential Diagnosis This is simple if the patient is over 3 years old for most patients with other severe cyanotic congenital abnormalities have died by this time Some forms of truncus arteriosus and pseudotruncus cannot be separated earlier The differentiation from the Eisenmenger syndrome is difficult since those cases of Fallot's syndrome with a slight pulmonary stenosis have very similar findings A complete transposition of the vessels will also have to be considered Pulmonary stenosis with atrial septal defect and patent ductus arteriosus with right to left shunt cause similar syndromes

Prognosis Surgery Most patients succumb early to the lesion although one man was known to reach the age of 59 years and a woman 64 years (Marquis) The impact of surgery on the duration of life cannot be estimated at present In the absence of dyspnea and squatting surgery is not justified There is no doubt that in patients with marked cyanosis dyspnea and convulsions marked improvement follows surgery The convulsions seem to be caused by a sudden marked right to left shunt and are treated by the administration of oxygen and Demerol

Three types of operation are in use First there is the Blalock Taussig operation now classical in which an arteriovenous fistula is created The pulmonary ischemia is improved by the creation of an anastomosis between the subclavian or the innominate artery and the pulmonary artery The operation is performed when there is evidence that a significant pulmonary circulation directly from the right ventricle is absent A pulmonary artery and systemic arteries as well must be present for the anastomosis The necessary pressure gradient must prevail in the arteries The mortality from this operation was at first about 18 per cent but soon fell to about 3 per cent in spite of great temporary improvement in individual survivors it should be kept in mind that one creates a large ductus arteriosus which strains the circulation and the heart A second operation was introduced by Potts and his collaborators in which the aorta is anastomosed side to side with the pulmonary artery Brock s procedure represents a third operation In this the pulmonary stenosis is attacked from the right ventricle This procedure is discussed in the section on pulmonary stenosis and should be the preferred method whenever feasible Surgery is preferably done when the patient is between the ages of 2 and 15

A follow up study by Potts et al of 100 children six to eight years after operation showed good results in 68 per cent and fair ones in 16 per cent Direct vision intracardiac surgery employing controlled crossed circulation has been used (*Lillehei et al*)

TRICUSPID ATRESIA

In this lesion a stenosis or atresia of the tricuspid orifice exists Blood reaches the left heart via a large atrial septal defect Blood reaches the lungs also with the aid of the bronchial arteries or a patent ductus arteriosus The right ventricle is very small and often is only rudimentary Pulmonary atresia or a ventricular septal defect may also be present

Patients with this lesion show a progressive general cyanosis from birth on Sometimes a peculiar unexplained paroxysmal dyspnea appears The heart is larger and a noncharacteristic systolic murmur is audible to the left of the sternum at the base of the heart A murmur may be missing Because of the larger left ventricle the apex beat may be heaving there is no pulmonary conus and the lungs are oligemic

In the electrocardiogram the P waves are large and there is a fairly characteristic left axis deviation in about 90 per cent of the patients This finding in cyanotic patients with a congenital heart lesion should arouse suspicion of the presence of a tricuspid atresia Rarely there is no axis deviation

Catheterization of the heart reveals that the blood pressure in the right atrium is high and that the oxygen content of the atrium is higher than that of the venae cavae because of the presence of an atrial septal defect The over all shunt of course is from right to left Angiocardiography shows small pulmonary arteries which are reached by the dye after opacification of the aorta The catheter

may be inserted into the left atrium and ventricle because of the septal defect

The success of the Blalock Taussig operation depends upon the size of the atrial septal defect

Ebstein's Disease

This congenital abnormality involves changes of the tricuspid valve While the anterior leaflet is often normally attached the rest of the leaflets particularly the posterior one is displaced downward toward the right ventricle The leaflets are usually fused to form a membranous structure which extends down into the right ventricle like a basket Parts of the leaflets are fused with the septum or the free wall of the ventricle Thus part of the ventricle is included into the right atrium and the actual right ventricle is small The ventricular portion proximal to the valves is very thin An atrial septal defect is usually present Often the leaflets do not arise from the annulus fibrosus but originate deeper Signs and symptoms depend to a large degree on the size of the atrial septal defect which is always present

Both dyspnea on exertion and palpitation appear early

These patients show cyanosis occasionally even at birth The heart is enlarged and clubbing is present However cyanosis may appear late and the circulation need not be changed much with mild deformities The pulmonary markings are often decreased Systolic apical murmurs and gallop rhythm over the apical area as well as arrhythmias are common The P R interval may be prolonged Paroxysmal tachycardia may occur (Brown et al) Tall P waves may also be observed Right bundle branch block is common

Roentgenography shows rather characteristic findings The right atrium is very large the aorta is narrow and the lungs are oligemic

Catheterization shows equal pressure in both atria and the catheter may be placed in the left atrium With the catheter in the right ventricle severe arrhythmias occur often

Angiocardiography shows a small right ventricle and a very large right atrium which empties slowly This examination is rarely necessary

Differential diagnosis should consider pulmonary stenosis with atrial right to left shunt atrial septal defect patent foramen ovale tricuspid atresia and Fallot's tetralogy

Ebstein's disease is not amenable to surgery One patient with Ebstein's anomaly reached the age of 79 (Adams and Hudson)

Congenital Aortic Stenosis

The occasional discovery of an atresia or stenosis of the aortic valves involving the conus the valvular area or the supravalvular part of the aorta was mentioned in the chapter on aortic stenosis This lesion is often combined with other congenital defects such as atresia of the mitral valve patent septa or patent ductus arteriosus

These rare abnormalities are caused by an abnormal development of the bulbus cordis

One should consider the possibility of this lesion when a rough systolic murmur is heard over the right second intercostal space in an infant This murmur may be transmitted to the cardiac apex The second aortic sound is often normal

PATENT DUCTUS APTERIOSUS

The ductus arteriosus (often named after Botallus although he was not the first to describe it) plays an important role in fetal circulation and usually closes functionally within a few weeks after birth Only in some cases does an opening remain after the third month of postfetal life Asphyxia seems to retard early closure (Kjellberg et al) One is permitted to speak of a 'persistent ductus arteriosus only if this link between the aorta and pulmonary artery persists for a longer time This lesion is much more common in females than in males Delayed closure may take place after the lapse of years

Incidence Among 88 cases of congenital heart disease discovered in school children the condition was found in 20 i e 23 per cent It has been estimated that at one time 20 000 adults in the United States had a persistent patency of the ductus arteriosus The incidence is said to be greater in the first born

Pathology The duct may be so short that there is practically only a fistula between the pulmonary artery and the aorta In other cases the duct is rather long It may be patent only for a bristle or wide enough to admit a thumb in the latter case paradoxical embolism may occur The diameter of the duct is greater at the aortic end than at the pulmonary end

Mechanism Owing to the high intra aortic pressure arterial blood is shunted into the pulmonary artery and therefore is forced to pass through the lungs for a second time While the flow is ordinarily directed from the aorta to the pul monary artery it may be reversed This happens not only in terminal stages but also when infants cry or suckle so that pressure in the lesser circuit rises a similar situation may arise when the lesion is combined with other defects The volume of blood shunted may vary from 4 to 19 liters per minute In spite of the enormous increase of blood flow in the lungs pulmonary arterial pressure may be normal With the development of an increased peripheral resistance in the lesser circuit and an increase of pulmonary arterial pressure a reversal of flow may occur with marked cyanosis often less pronounced in the head and right arm

Symptoms and Signs These depend chiefly upon the width of the communi cation Patients with a patent ductus arteriosus may lead an active life without any handicap if the opening is small Complaints may appear early (even in childhood) and the diagnosis is easier when the communication is broad Cyanosis and polycythemia should arouse the suspicion of a complication The growth of the patient is delayed Fatigue dyspnea palpitation and chest pain occur

The diagnosis is not always easy and — particularly in cases in early child hood — may present great difficulties

When regurgitation is considerable it may amount to 75 per cent of the output of the left ventricle This results in a water hammer pulse capillary pulse and a low diastolic blood pressure as in aortic regurgitation

A systolic (rarely a diastolic) thrill is palpable over the pulmonary artery Cardiac size may be normal unless a large communication causes right and left ventricular dilatation The pulmonary artery is markedly dilated if prominent on the left cardiac border it causes neutralization This was known in older literature as Gerhardt s ribbon dullness The conus of the pulmonary artery is not always pronounced Often the heart is normal in size and the left atrium may be slightly enlarged

With small communications a systolic murmur is often heard in the second intercostal space to the left of the sternum (Gibson s murmur) This is the only auscultatory finding even with broad communications in children up to the fourth or fifth year of life A diastolic apical murmur may appear even in the first month of life In persistent right aortic arch a diastolic murmur is heard to the right of the sternum Later in typical cases there is a continuous systolic and diastolic murmur with systolic accentuation (machinery murmur) due to the fact that blood is shunted from the aorta into the pulmonary artery in systole as well as in diastole The second pulmonic sound is accentuated and the pulmonary vessels may show evidence of increased pressure In some cases no murmurs are audible if pressures in the aorta and pulmonary artery are equal

As in aortic insufficiency anginal pain may appear

At times the x ray picture of the heart is similar to that of a patent atrial septum or an incomplete pulmonary stenosis The lung fields showing pleonemia or oligemia respectively permit the diagnosis

The electrocardiogram is often normal since the increased burden is laid upon the right *and* left ventricles hypertrophy of both in a more or less parallel manner may prevent the appearance of an axis deviation

Catheterization Angiocardiography The best sign is passage of the catheter through the duct The oxygen saturation of the blood in the pulmonary artery is greater than in the right ventricle Angiocardiography sometimes shows a small filling defect in the pulmonary artery because of the mass of arterial blood shunted from the aorta The dye may be found for an abnormally long time in the lesser circuit The ductus itself may sometimes be observed in the left anterior oblique position A diverticulum like dilatation is sometimes seen in the aorta at the orifice of the ductus Retrograde aortography leads to an early filling of the pulmonary artery

Differential Diagnosis The distinction from an atrial and ventricular septal defect and from a venous hum in anemia must be considered

Even if all the characteristic signs seem to be present one must take care not to confuse the lesion with an aortic pulmonary septal defect a left ventricle right atrium shunt in a high interventricular septal defect or rupture of an aneurysm of the right aortic sinus into the right ventricle or arteriovenous pulmonary fistula

The diagnosis is more difficult when only a systolic murmur is present

Complications About 30 to 40 per cent of the patients used to succumb to subacute bacterial endocarditis This lesion is usually located around the duct and in the wall of the pulmonary artery where blood from the aorta strikes the vessel Approximately 15 per cent develop a pulmonary aneurysm which may rupture

Another large group of patients develops congestive heart failure Never theless patients may reach the age of 60 without awareness of the lesion and survival to 79 years is known Congestive heart failure develops early when all signs are distinct A patent ductus may close spontaneously

The combination of patency of the ductus arteriosus with other lesions is common In some cases of stenosis of the pulmonary valves for instance patency of the ductus arteriosus is a necessary complication to prolong or even to maintain life In patients who live beyond childhood uncomplicated ductus arteriosus is however the rule

Reversed blood flow from the pulmonary artery into the aorta due to pul monary vascular changes is a serious complication These changes (fibrous intimal proliferation) are sometimes present at birth

Surgery The diagnosis of patency of the ductus arteriosus has assumed importance since as Gross showed (1939) the duct may be successfully closed by ligation

The decision to operate on a patient with a patent ductus arteriosus is fraught with difficulty One must at first rule out the existence of other congenital lesions Complications during or immediately after the operation create a mor tality of about 5 per cent when all cases operated on are included In experienced hands the operation results in a mortality that is now less than 1 per cent Some of the earlier patients succumbed to acute infections this is prevented at pre ent by administration of penicillin Occasionally the duct is very short and for practi cal purposes an arteriovenous fistula between the aorta and pulmonary artery exists In these cases ligation is impossible but successful surgery has been done

Patients with patent ductus arteriosus should be carefully watched and the operation performed between the ages of 6 and 12 years If the patient is 35 years or older and in good condition operation is unnecessary Moreover no surgery should be undertaken in patent ductus arteriosus with a reversed flow since the high pressure in the le ser circuit often leads to acute right heart failure

The danger of operation on the other hand is opposed by the ever present possibility of the development of subacute bacterial endocarditis and decom pensation Therefore every case must be judged according to its own merits It is however clear that patients who had subacute bacterial endocarditis impending decompensation or those with marked enlargement of the right and left ventricles need operative intervention Complete cure has been reported repeatedly following the operation in cases already complicated by subacute bacterial endocarditis The operation should not be undertaken in children under the age of 6 years since delayed spontaneous closure does occur The clearer the

evidence is that a wide communication exists with marked shunting of blood (low diastolic blood pressure enlargement of the heart) the more likely a shortened life and the clearer the indication for operation

The persistence of murmurs of a patent ductus arteriosus after its ligation is an interesting problem Actually ligation does not obliterate the duct and does not prevent the formation of eddies It is probable however that in patients in whom a diastolic murmur persisted the duct has not been successfully ligated Recanalization has occurred with simple ligature in 10 per cent of the cases operated on This reason plus the added fact that a pulmonary aneurysm may be present has made division of the duct and careful suture of both ends the method of choice

COARCTATION (ISTHMUS STENOSIS) OF THE AORTA

Incidence This interesting anomaly a narrowing or complete occlusion of the aorta after the departure of the large arteries is not as uncommon as many believe It is said to occur in one of every 1000—1 500 necropsies

The malformation is 4 to 5 times as common in males as in females Although it is often overlooked the diagnosis is easy if a search for certain signs is made The lesion has been observed in brothers (Klemola)

Pathology Two varieties are recognized In the infantile type the stenosis involves the aortic isthmus between the origin of the left subclavian artery and the ductus arteriosus Sometimes this part of the aorta is converted into a fibrous cord The ductus arteriosus is usually patent the circulation in utero persists and there is no collateral circulation Often additional malformations coexist The lesion is serious and afflicted children die within one year

The adult type consists of a short narrowing or atresia at before or just below the insertion of the ductus arteriosus which is usually but not always closed The amount of stenosis varies considerably and milder grades are compatible with long life In one oft cited patient death occurred in the ninety second year A narrowing of the aorta in this area for 1—2 mm occurs physiologically

Since the time of Skoda the development of the lesion has been associated with the physiologic closure of the ductus due to an extension of the obliterative process of the ductus into the aorta Some facts speak against this conception Thus the ductus may be patent in some cases of coarctation of the aorta An abnormal junction or abnormal regression of the primitive branchial arteries is responsible

Not rarely there is complete occlusion (atresia) The lesion may occur far down in the thoracic aorta and even in the abdominal aorta down to the iliac arteries The aortic valves are bicuspid in 25 to 40 per cent of the cases In 10 per cent the aorta is hypoplastic If the ductus arteriosus is patent and brings venous blood into the aorta the oxygen saturation of blood in the head and upper extremities is normal but in the lower extremities it is subnormal These parts may be cyanotic

The diagnosis is more difficult when only a systolic murmur is present

Complications About 30 to 40 per cent of the patients used to succumb to subacute bacterial endocarditis This lesion is usually located around the duct and in the wall of the pulmonary artery where blood from the aorta strikes the vessel Approximately 15 per cent develop a pulmonary aneurysm which may rupture

Another large group of patients develops congestive heart failure Nevertheless patients may reach the age of 60 without awareness of the lesion and survival to 79 years is known *Congestive heart failure develops early when all* signs are distinct A patent ductus may close spontaneously

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FIG. 58. Notching of the ribs in a patient with coarctation of the aorta

The mechanism of the hypertension is still disputed Animal experiments suggest that this is not due to mechanical factors but to an interference with the blood supply to the kidneys which causes the release of pressor substances If this were the case an increased pressure should also be expected in the lower extremities There is some evidence that peripheral vasoconstriction is general in these cases Unknown mechanisms may also interplay The blood pressure *may remain elevated after successful therapy but any elevation of blood pressure* may persist even after removal of the cause

Coarctation of the aorta should always be suspected when high blood pressure is detected in a young individual and is not readily explained by a positive family history of hypertension

As stated earlier the absence of a femoral pulse should always make one suspicious of an aortic coarctation in an adult In children however the femoral artery may pulsate (Gruner and Herbst)

The electrocardiogram often shows left axis deviation and evidence of left ventricular hypertrophy

Roentgenography The diagnosis is usually established by characteristic x ray findings In the left anterior oblique position a defect in the aortic outline can be seen

Very important are the erosions of ribs As the result of the widening and the strong pulsations of the intercostal arteries erosions appear on the lower part of some of the ribs these can be easily demonstrated (figure 58) The erosions are absent from the first two ribs and they may be missed in the last three They *are present in about 75 per cent of patients with coarctation The scalloping* is due mainly to the tortuosity of the arteries actually it is not on the lower border of the ribs but is found at the junction between the main bodies of the ribs and the thin portion that forms the costal groove This abnormality has also been seen unilaterally in other lesions (tetralogy of Fallot) Notching of the ribs on the left side alone occurs when the right subclavian artery arises distal to the coarctation or when this artery is stenotic (Love and Holms) Right sided notching appears with coarctation of the aortic portion between the left carotid and left subclavian arteries Notching of the ribs develops after division of the subclavian artery after Blalock s operation for pulmonary stenosis (Kent) Rib notching has been seen in a baby five months old (Gruner and Herbst) but usually appears in 6 to 10 year old patients In neurofibromatosis with participation of the intercostal nerves notching of the ribs may be observed

Tomography may also show the stenotic area

The vascular shadow is often deformed The widened left subclavian artery may cause a bilobate shadow on the upper left cardiac border The upper lobe is formed by the aorta the lower lobe by the subclavian artery The aortic knob may be absent and it may appear bilobate owing to the widening of the post stenotic aorta The widened left subclavian artery may be confused with the aortic arch

Abnormal esophageal patterns due to kinking of the aorta because of post stenotic dilatation occur (Figley) Bruwer describes a notch in the left border of the descending aorta above the level of the pulmonary artery it occurs in one third of the patients with coarctation In lateral x ray pictures the widened mammary arteries are visible (Odmann)

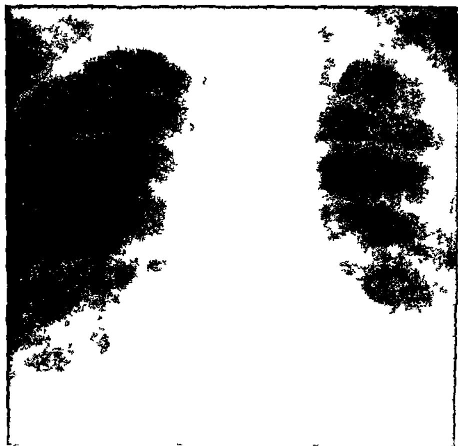


FIG 59 Retrograde aortography reveals coarctation of the aorta in a 23 year old woman

Further Comments In 24 of 40 patients with coarctation Grantstrom found corkscrew tortuosities of the retinal arteries

When coarctation develops proximal to the ductus arteriosus no adequate collateral circulation develops before birth (Bahn et al)

The lesion is often combined with other anomalies such as a bicuspid aortic valve and abnormal origin of the left subclavian artery

By virtue of the impaired blood supply the development of the lower half of the body may be somewhat retarded in contrast to the upper half thereby resulting in a body that is malproportioned The discrepancy may also be evident in the color and temperature of the two regions

Ballistocardiogram This often shows a decreased length or absence of the K wave which is caused by the impact of the ejected blood into the aorta This sign however is also found in thrombosis of the abdominal aorta (Leriche syndrome) On the other hand deep K waves have occasionally been found in patients with coarctation

Catheterization and Angiocardiography Cardiac catheterization does not contribute to the diagnosis Intravenous angiocardiography is also often of little value since the dye has been diluted too much by the time it reaches the aorta The best method is to inject the contrast medium directly into the pulmonary artery or right ventricle Retrograde aortography with local deposition of the dye has been attempted The stenosis is then visualized when the patient is in the left anterior oblique position (figure 59)

Complications Many patients die of left ventricular failure In 40 of 200 cases spontaneous rupture of the heart or aorta above the stenosis caused death The aorta may rupture directly into the pericardium or a dissecting aneurysm may form Mycotic endaortitis and cerebral hemorrhage also are common Aneurysms of the circle of Willis are not rare Consequently the patient should not perform heavy physical labor

A mitral stenosis occasionally coexists

Prognosis It has been found that 25 per cent of the patients may attain a fairly old age 25 per cent develop subacute bacterial endocarditis (aortitis) and 25 per cent have rupture of the aorta Others die from cerebral hemorrhage or decompensation It is estimated that 61 per cent die before the age of 40

Surgery Removal of the stenotic area and end to end anastomosis of the aorta was performed for the first time by Crafoord and Gross in 1944 The mortality from this operation is now less than 5 per cent The operation is not undertaken if the blood pressure is normal Moreover surgery is seldom performed in patients beyond the age of 30 years since the aorta at this age has lost much of its elasticity so that an end to end anastomosis is not feasible If the section of the aorta removed is long and the two ends cannot be reunited a graft of homologous aortic tissue is used The operation is not performed in childhood since the lumen of the operated area will not widen as the patient grows After a successful operation the blood pressure gradually falls but not always to normal levels Improvement is slow and does not follow surgery immediately At times patients 40 years of age have been improved while others only 20 years of age failed to respond to operation (Hallenbeck et al)

ABNORMALITIES OF THE AORTIC ARCH AND ITS GREAT ARTERIES

There are a large number of variations of abnormalities in this area (Edwards et al) but they require no description in this book However since some of them have serious consequences when they compress the trachea and esophagus they will be briefly mentioned at this juncture

During the development of the aorta and the pulmonary artery with their branches certain arterial arches (branchial arteries gill arteries) appear and

disappear There are six arteries of this kind on each side but all are never present at the same time The aortic arch normally develops from the left fourth branchial artery while the right one undergoes obliteration If the right fourth branchial artery and the left one persist the aortic arch is double Usually however a larger part of the left arch vanishes and a persistent right aortic arch results

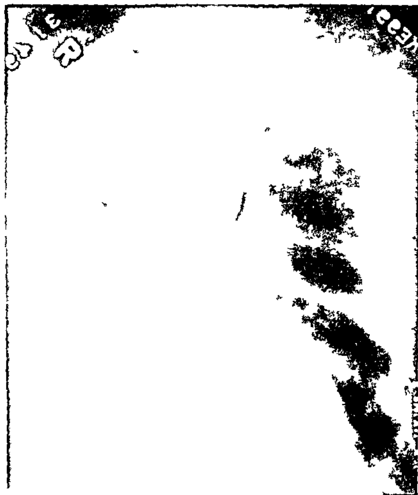


Fig 60 Abnormal esophageal pattern in a patient with persistent right aortic arch (p a picture)

This condition is not rare but since it causes no symptoms in the majority of cases discovery is accidental on occasion of an x ray examination Other anomalies such as coarctation of the aorta often coexist

Many variants are known which depend mainly on how much of the left aortic arch persists and on the site of origin of the left subclavian artery The

persistent right aortic arch rides the right main bronchus and then proceeds forward and to the left usually behind the trachea and the esophagus

The typical x ray picture consists of the absence of the usual aortic knob and its appearance on the right side or bilaterally with the descending aorta at

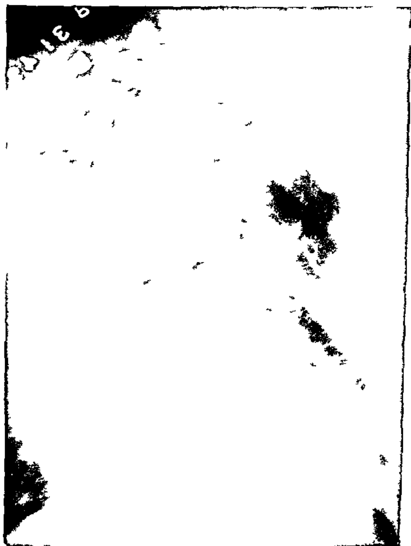


FIG 61 The esophagus is displaced forward in the right anterior oblique position (persistent right aortic arch)

the right upper cardiac border If the esophagus is filled with barium the convexity of the aortic impression in the esophagus in the postero anterior position is directed not to the right which is normal but to the left (figure 60) In the right anterior oblique view the esophagus and trachea are displaced forward by the aorta which swings behind it from right to left (figure 61) The aorta may be

widened and may form a diverticulum at this place Compression of the esophagus by the vascular rings may cause dysphagia (dysphagia lusoria) Death has resulted from compression of the trachea and esophagus In some cases the ductus arteriosus originates on the right side from the aorta and travels behind the esophagus and trachea to the pulmonary artery on the left side The aortic rings may be patent or fibrotic

Dysphagia may also be a symptom if the right subclavian artery arises at a point distal to the origin of the left subclavian artery and crosses to the right between the esophagus and the vertebral column

TRANSPOSITION OF THE GREAT ARTERIES

If the development of the bulbar part of the ventricles is disturbed and there is an abnormal torsion in this area a transposition of the pulmonary artery and aorta results This is usually combined with other abnormalities especially with ventricular septal defects Several subvarieties are recognized

The defects are interesting because they are not explained by a mere disturbance of development In ontogenesis no stage is reached in which similar conditions prevail According to the phylogenetic theory of Spitzer the lesion results from an arrested development in the early phase with the heart adapting itself to this disturbance

Type I The *riding aorta* originates from the right *and* left ventricle over a large ventricular septal defect This form has been discussed previously in connection with the Eisenmenger and Fallot syndromes Since according to Spitzer torsion of the primitive cardiac tube is one of the requirements of the formation of the interventricular septum abnormal torsion leads to a septal defect

Type II *Simple transposition* is an anomaly in which the pulmonary artery and aorta originate from the right ventricle a septal deficiency coexists

Type III In *complete transposition* the aorta arises from the right ventricle and the pulmonary artery from the left These patients must also have a large atrial or ventricular septal defect or a patent ductus arteriosus to live

The lungs are pleonemic since the pulmonary artery arises from the left ventricle The ascending aorta is situated anteriorly to the left while the pulmonary artery is posterior to the right There is pronounced cyanosis from birth The patient very rarely reaches adult life There is progressive neonatal cardiac enlargement

Type IV *Mixed transposition* is a term applied when in addition to the changes in type III the right ventricle contains only the aortic orifice while the tricuspid orifice is included in the left ventricle

In the Taussig Bing syndrome the pulmonary artery rides over both ventricles and the aorta originates in the left ventricle

In *corrected transposition* the aorta and pulmonary artery originate from the proper ventricle but their position in respect to each other is changed The aorta is situated ventrad to the pulmonary artery (see next section)

Severe cyanosis and clubbing is the rule Murmurs may be absent Deformities of the chest and kyphosis are common

Attempts have been made to improve the circulation of patients with transposition of the great vessels by surgery

DEXTROCARDIA

The heart may be located in the right chest owing to displacement by pulmonary disease effusions diaphragmatic hernia or high position of the left diaphragm (dextroposition of the heart) In true dextrocardia two main groups are differentiated

(1) *Dextrocardia with complete inversion of the viscera* (situs inversus totalis) In these patients the organs are properly located except they form the mirror image of the normal the situs solitus Other congenital anomalies are rare they may occur just as they do in other individuals Inversion of all main waves of lead I in the electrocardiogram is characteristic for this lesion The anomaly is an accidental finding without practical importance

(2) *Isolated dextrocardia with normal or partly abnormal position of the abdominal viscera* Usually other congenital abnormalities and variations are present In some variants the position of the heart chambers is normal but the axis of the heart is changed from left craniad to right caudad (dextroversion of the heart or dextrotorsion after Zdansky) At other times the position of the atria and great vessels seems normal but the ventricles are transposed If a complete transposition of the aorta and pulmonary artery coexists the lesion is corrected in an ideal manner (corrected transposition as mentioned in the previous section)

In all these varieties the electrocardiogram may be normal or show atypical alterations

ARTERIOVENOUS FISTULA

Systemic Circulation

Pathology Communications between the peripheral arteries and veins similar to the abnormal connection in persistent ductus arteriosus have been known since William Hunter described the acquired variety A number of other names have been bestowed upon the lesion the most popular being arteriovenous aneurysm in some instances the appearance has led to such descriptive terms as cirsoid cavernous racemose aneurysm and the like The communications are classified into two types congenital and acquired

The congenital variety is found in the neck or the extremities Usually there is a lateral anastomosis due to the presence of small communicating vessels but sometimes an end to end anastomosis exists between arteries and a venous plexus Often several anastomoses are present

The acquired arteriovenous fistula is found anywhere in the body where trauma creates a communication between an artery and vein

Signs The general effect is that blood is forced under arterial pressure directly into the venous system This causes changes in the vessels so that the artery may become venified and the vein arterialized If the fistula happens to be located in an extremity extreme engorgement and dilatation of the veins may be seen and ulceration of the skin may occur at times Occasionally the veins are so dilated that an operation is performed for the supposed varicose veins — with disastrous results The circumference of the affected extremity may be increased while the bones are so enlarged as the result of increased vascularity that local gigantism develops Since the resistance to the flow of blood through the fistula is less than to the flow through the capillary bed large volumes of blood may be attracted to the area with consequent dilatation of all nearby vessels as a result a local increase of skin temperature appears as a common sign of increased vascularity

A characteristic bruit and thrill are often present they are most pronounced over the fistula and are transmitted distally and proximally along the course of the affected vein Pressure on the site of the fistula as well as on the proximal section of the artery causes the murmur as well as the thrill to vanish If an intracranial fistula is present the patient as well as the examiner may hear the bruit

The development of varicose veins at an abnormal location early in life should make the examiner suspicious of the presence of an arteriovenous fistula Arteriography assists in the diagnosis

In the acquired type the artery and vein are usually penetrated by a foreign body — a bullet knife splinter of glass and so forth Usually the original hemorrhage is easily controlled however the arterial pressure produced in the vein may cause enormous edema and gangrene may necessitate early amputation of the extremity Some patients die immediately due to cerebral or myocardial anoxia *Frequently the attendant shock and acute hypotension preclude the* immediate appearance of a bruit and the thrill These signs become obvious with the improvement in the general condition of the patient The bruit and thrill are continuous throughout the cardiac cycle and a systolic accentuation often occurs

The other peripheral signs are the same as in aortic insufficiency and patency of the ductus arteriosus There is a water hammer pulse and a low diastolic blood pressure The systolic blood pressure may be elevated presumably owing to the increased cardiac output The size of the heart is increased for cardiac strain is augmented about one fifth to one half of the output may leak into the veins The left ventricle dilates for reasons that are not entirely clear some investigators claim it is caused by a reduction of coronary blood flow but we question this explanation It is also not entirely clear why dilatation of the heart is usually absent in the congenital type of lesion The early adaptation of the circulation to the lesion may play a role *Decompensation may occur in the* acquired type just as it happens in a patent ductus arteriosus

Fluoroscopy may show that compression of the fistula and the arrest of leakage diminish the size of the heart in the acquired type During compression—

the heart rate diminishes 20 to 30 beats per minute and the blood pressure falls 20 to 30 mm Hg (Branham s sign)

Surgery If the patient is seen immediately after the development of the fistula suturing with restoration of the vessels may be considered When some time has elapsed delay in operation is justified since small fistulas may heal spontaneously also procrastination permits the development of some collateral circulation with less likelihood of gangrene if ligation of the main vessel is necessary However if dilatation of the heart has occurred spontaneous closure is very unlikely and operation is necessary (Holman)

Surgery offers great assistance in restoring normal conditions In some cases subacute bacterial endarteritis develops at the site of the fistula and can be cured by operative intervention Subacute bacterial endocarditis may also develop at the usual sites on the cardiac valves (see section on subacute bacterial endocarditis)

The previous discussion is applicable chiefly to the ordinary arteriovenous fistula of an extremity Naturally the situation is somewhat different when the fistula joins large vessels within the thorax or when the internal carotid artery and cavernous sinus are joined following fracture of the sphenoid

These problems belong to the domain of surgery and will not be discussed in detail here

Obviously the clinical picture is modified by the character of the tissue supplied or drained by the involved vessels Thus in arteriovenous fistula involving the internal carotid artery and cavernous sinus there is stabbing knife like retroorbital pain pulsating exophthalmus an audible bruit and a variety of visual disturbances In other lesions involving the carotid or vertebral arteries we have observed the gradual development of neurologic and psychiatric syndromes Whether or not surgery should be undertaken will depend upon the individual circumstances for ligation of a carotid artery for example may be followed by contralateral hemiplegia in a middle aged subject If the vessel can be compressed for an hour without the appearance of headache or weakness and tingling in the contralateral extremity constriction of the involved vessel by fascia lata may be considered

Lesser Circulation

Congenital arteriovenous fistula in the lesser circulation is a condition related to familial hereditary hemorrhagic telangiectasia (Rendu Osler Weber) It is also seen in several members of the same family but the skin and mucous membrane lesions are often missing Sometimes the lesion is bilateral It consists of a short dilated afferent artery and several dilated efferent veins with many distended vessels inbetween Secondary focal degenerative processes take place in the convolution of the vessels and added communications between veins and arteries appear This abnormality involves males as a rule and is usually recognized before the thirtieth year of life

Symptoms The chief symptoms are dyspnea and hemoptysis Petrosternal pain and epileptiform attacks occur in some cases There is dizziness faintness and attacks of uncon ciousness as well as epistaxis and headaches Some symptoms are due to anoxia and some depend upon the polycythemia

Signs The outstanding sign on physical examination is a murmur that is often continuous from systole to diastole with a systolic accentuation it becomes louder on deep inspiration and is often heard over the back

Roentgenography shows an abnormal shadow most often in a lower lobe It often enlarges on Mueller s experiment and diminishes in size during a Valsalva experiment The heart is often normal in size

Tomography reveals the dilated efferent veins as a wormlike shadow and angiography is rarely necessary There is marked polycythemia with as many as 11 million red blood cells per cubic millimeter Often the fingers are clubbed and pulmonary osteoarthropathy may appear Oxygen saturation of the blood falls to 60 per cent

Differential Diagnosis At times it may be difficult to distinguish the lesion from polycythemia vera However the spleen is not enlarged and there is no leukocytosis

Therapy Lobectomy cures the disease Occasionally this also holds for certain acquired arteriovenous fistulae of the lung Thus we have occasionally encountered an acquired lesion following ill performed thoracentesis when the lung was entered and an artery and vein transfixed This accident may be reported with increasing frequency if the current popularity of pleural and lung needle biopsy persists

ENDOCARDIAL FIBROELASTOSIS

This anomaly is found in newborns and in infants although the lesion has been seen in patients over twenty years old The children suddenly develop dyspnea fainting and collapse cyanosis during crying and tachycardia appear The patients die suddenly often within 24 hours There is terminal cyanosis and the blood pressure is very low There are no characteristic findings on physical examination and the electrocardiogram often shows abnormal T waves and slurring as well as notching of the QRS complexes These signs however are not pathognomonic Complete heart block has been noted Most patients die before they complete their second year of life A few patients reach the age of 24 (Panke and Pottino) or older

Postmortem examination reveals a marked endocardial fibrosis which according to some prevents sufficient cardiac diastole just as happens with constricting pericarditis

A variety of factors have been suspected to be etiologic Inflammation fetal endocarditis and chronic anoxia have been held responsible The fact that siblings have suffered from this illness and the concurrence of other congenital abnormalities tends to support the theory that a malformation is responsible for this anomaly

THERAPY OF CONGENITAL HEART LESIONS

Treatment has been mentioned in connection with the various lesions In addition to the suggestions offered regarding the aforementioned measures the following general remarks may be made Physical strain should be avoided Good over all hygiene may prolong life for many years in patients with congenital heart lesions In the cyanotic group especially in patients with polycythemia repeated small phlebotomies help

Great care must be taken to avoid infection of the teeth or tonsils If present such infections should be treated with antibiotics as a prophylaxis against sub acute bacterial endocarditis Some of these patients die of brain abscesses an additional indication for antibiotic therapy For sudden attacks of anoxia, the knee chest position may help

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Chapter 16

Anginal Pain and its Differential Diagnosis

Nomenclature

A discussion of angina pectoris must be preceded by some remarks concerning nomenclature since the latter is rather confusing and needs clarification. The nomenclature of diseases is closely associated with our knowledge of their etiology or mechanism. In the past there has been much confusion with respect to the explanation of angina pectoris. Huchard alone counted 80 theories designed to explain its cause. On the other hand, few other subjects in medicine have experienced equally great progress in recent years. It is our impression that nomenclature has not quite kept pace with this progress. Since the classical work of Heberden, the term "angina pectoris" was and still is widely used to define a disease entity. Heberden's description of certain sensations was so brilliant that little was added for a long time, with the result that "angina pectoris" came to signify the same disease to every physician.

That the basic mechanism underlying the condition probably is always the same — hypoxia of the heart muscle — has been suspected by many clinicians since Parry. Potain compared angina pectoris with intermittent claudication. Scientific progress in the last twenty years, however, has demonstrated that hypoxia of the heart muscle may be produced in a number of ways and that these variegated conditions have a different prognosis and require different management. Therefore, it seems advisable to use the term "angina pectoris" only to define a *symptom*. The etiologic mechanism causing the angina pectoris should always be added.

The classical anginal syndrome (angina on effort) for which the term "angina pectoris" is widely used at present, in the majority of cases derives from a well defined lesion of known etiology, that is, an atherosclerotic or syphilitic stenosis of the coronary arteries or their orifices. Therefore, the term "atherosclerotic or syphilitic coronary stenosis with angina pectoris" seems more appropriate to us than the unqualified "angina pectoris."

The term "angina pectoris" as a name for a disease entity need not be retained for historical reasons since Heberden's clinical description also includes attacks which at present would undoubtedly be attributed to coronary occlusion. In describing the pain he states ... and "I have met with one in whom it continued for several days" and "If it comes on in the night it will last for an hour or two." These patients obviously did not have a simple angina pectoris

In recent years the term coronary insufficiency has found wide usage This term is intended by some to designate a situation somewhat between angina on effort and coronary occlusion The myocardial ischemia is more prolonged than in angina on effort and therefore may lead to slight anatomic changes Others understand coronary insufficiency to mean a chronic status of diminished blood supply to the heart muscle Still again others proposed different definitions We regard the term as a rather unfortunate designation as will be pointed out To begin with the name is incorrect because it is the coronary blood flow and not the coronary artery which is insufficient In patients with anemia or carbon monoxide intoxication the flow of blood is not abnormal but all signs of coronary insufficiency are present It is true that the phrase aortic insufficiency is employed in a similar way when an insufficiency of the aortic *valve* is meant this usage is excusable when everyone uses this term to define the same condition Apparently this is not the case in coronary insufficiency or coronary *failure for these designations are applied when the heart muscle obtains* insufficient amounts of oxygen because of carbon monoxide poisoning anemia pulmonary embolism or paroxysmal tachycardia It cannot be assumed that the same coronary insufficiency is operating in all these conditions Coronary insufficiency is not a diagnosis

We shall see that many instances of so called coronary insufficiency actually concern small myocardial infarctions due to occlusion of small vessels this will be discussed in a later section In some instances infarctions occur because of a combination of a mere coronary stenosis with overexertion or tachycardia

We consider the term coronary insufficiency permissible only if it is used to define a pathophysiologic state and is further qualified e g coronary insufficiency due to acute hemorrhage coronary stenosis caused by a syphilitic aortitis and so forth It is not a term to indicate a certain illness

In the following chapters the term angina pectoris or anginal pain will be used to define a pain caused by hypoxia of the heart muscle The various conditions in which this type of pain may occur will be described In an endeavor to apply in this field of cardiology a nomenclature based on etiology — a procedure so successfully promoted by the New York Heart Association for other cardiovascular diseases — we will discuss angina pectoris as a symptom occurring in a variety of conditions The term will not be used to describe a disease entity The phrase coronary insufficiency as a diagnosis is not used at all

ANATOMY AND PHYSIOLOGY OF THE CORONARY CIRCULATION

ANATOMY OF THE CORONARY ARTERIES

The right coronary artery originating in the right sinus of Valsalva runs in the atrioventricular sulcus to the posterior aspect of the heart and forms the descending posterior branch in the posterior interventricular sulcus It supplies two thirds of the *posterior aspect* of the right ventricle but it does not nourish

the area of the right ventricle near the anterior interventricular sulcus Further more it supplies the right margin of the heart and the inferior or basal portion of the left ventricle posteriorly It is also responsible for supplying the right atrium and the posterior third of the interventricular septum Important branches are sent to the sinus node the atrioventricular node the bundle of His and the bundle branches

The left coronary artery is usually wider than the right It originates in the left sinus of Valsalva and divides into two main branches One branch the left circumflex artery supplies the left margin of the left ventricle and most of the left atrium The descending branch of the left coronary artery runs in the anterior interventricular sulcus and supplies the anterior part of the left ventricle as well as adjoining parts of the right ventricle It also nourishes the anterior two thirds of the interventricular septum Approximately 40 per cent of people have a branch of the left coronary artery which supplies the sinus node

While this description of the blood supply holds for nearly 90 per cent of normal subjects exceptions and variations occur in 10 per cent They are most common in the circumflex branch of the left main coronary trunk This vessel occasionally supplies larger parts of the basal and posterior aspects of the left ventricle

Thickening of the intima of the coronary arteries is a sign of aging In childhood the intima is already as thick as the media and in the aged the intima is several times as thick as the media

Congenital abnormalities of the coronary arteries such as a single coronary artery for the whole heart more than two coronary orifices and origin of a coronary artery from a pulmonary artery are frequently observed

The left more rarely than the right (or both) coronary arteries can arise from the pulmonary artery (Soloff) This may be compatible with life up to 60 years when sufficient anastomoses between the two coronary arteries exist but it often is associated with sudden death early in childhood The children show pallor perspiration cyanosis or dyspnea The heart is enlarged and gallop rhythm is often present The T wave in the electrocardiogram is deeply inverted in lead I and sometimes also in lead II The T waves in the chest leads are also inverted but this is often seen under normal conditions in children

A single coronary artery is usually compatible with a normal function but it creates a dangerous situation when coronary occlusion occurs

Absence of coronary orifices has been seen in a child 14 months old (Grant) where the necropsy revealed blood filled spaces which communicated with the lumen of the ventricles and the coronary vessels

An interesting instance of an anomalous left coronary artery which communicated directly with the right ventricle and caused a machinery murmur of a patent ductus arteriosus has been reported (Davis et al)

Congenital or mycotic aneurysms of the coronary arteries occur and are often multiple

Complete obstruction of the coronary sinus vein does not seem to exert an adverse influence on cardiac activity (Grant)

ANASTOMOSES

Anastomoses between the branches of the two coronary arteries are numerous Normally they are too small to function satisfactorily if one of the communicating vessels is suddenly occluded The coronary arteries are therefore called functional end arteries Hypoxemia anemia and the use of nitrites enhance (in the experimental animal) the widening of anastomoses The normal physiologic anastomoses are not wider than 40 micra The anastomoses are said to increase with advancing age but this fact is denied by others Anastomoses widen with a slowly progressive stenosis of one of the branches

Thebesian Vessels The existence of thebesian veins has often been denied but careful studies have confirmed their existence and provided detailed knowledge of the anatomy The coronary arteries communicate with the thebesian vessels only through the capillaries The thebesian vessels are particularly numerous in the right ventricle This circumstance together with the more abundant anastomoses between the coronary arteries within the right ventricle contribute to prevent damage in this ventricle in coronary artery diseases Even if a complete occlusion of a coronary artery supplying the right ventricle occurs it is rarely accompanied by infarction in the right ventricle

Arterioluminal and Arteriosinusoid Vessels Important communications between the coronary arteries and the ventricular cavities are provided by the arterioluminal and arteriosinusoid vessels The former were noted by Vieussens they originate from the arterioles and have a diameter up to 1 mm They are not abundant but provide a short circuit from the arteries direct to the ventricles The arteriosinusoid vessels also begin in the arterioles but they break into wide tubes of irregular shape they are very numerous and have a capillary like structure Not much information has been obtained concerning the function of these communications under normal or abnormal conditions

Extracardiac Anastomoses The coronary arteries also communicate with extracardiac arteries Most numerous are the anastomoses between the coronary arteries and the vasa vasorum of the aorta and the pulmonary artery The first portion of the ascending aorta is nourished by vasa vasorum originating from the coronary arteries particularly from the right coronary artery These extracardiac vessels may attain remarkable size and they certainly play a great role in nourishing the heart when the main branches of the coronary arteries undergo slow occlusion Furthermore the coronary arteries communicate with the pericardial diaphragmatic pulmonary and esophageal arteries

It is possible for aortitis to occlude both coronary orifices completely without impairing cardiac function and without the development of myocardial infarction This speaks in favor of the functional capacity of the cardiac and extracardiac anastomoses

CARDIAC NERVES

Adrenergic sympathetic fibers are found throughout the myocardium There is however no anatomic or experimental proof that inhibitory vagal effects exist in the mammalian ventricles with the exception of the vasoconstrictor fibers of the coronary arteries Vagal fibers are found in the atria of all animals and in the ventricular muscle of many lower animals but have apparently disappeared in the course of evolution in the ventricle of mammals A teleologic explanation of this fact is obvious Animals with inhibitory vagal fibers in the ventricle did not long survive the stresses of life

CORONARY BLOOD FLOW

Blood Pressure On the basis of experiments with denervated heart lung preparations it was long believed that coronary blood flow depended exclusively on mean aortic pressure Investigations on hearts with intact nerves and improved technique however have shown that this is not the case A priori sole dependence of coronary blood flow from aortic pressure was unexplainable for it was known that coronary blood flow can increase multifold on exertion whereas the blood pressure increases only slightly

The heart behaves like other organs of the body in regard to its arterial blood flow It takes the quantity of blood needed from the aorta and does this within limits quite independently of the blood pressure It is not passively perfused Under normal conditions about 5 to 10 per cent of the cardiac output is taken by the coronary arteries and this amount increases decidedly during exertion Widening of the coronary arteries is accomplished mainly by reflexes and partly by the action of local metabolites

Autonomic Nerves The denervated heart always shows a maximal coronary blood flow Therefore continuous nerve tonus may be assumed to control the width of the coronary vessels in the heart in situ and to permit changes in accordance with momentary needs At present there is wide agreement that the vasoconstrictors for the coronary arteries arise in the parasympathetic system and that the adrenergic vasodilators are provided by the sympathetic system While some investigators conclude from their experiments that an increase or decrease of the tonic vagal innervation is chiefly responsible for alteration of coronary blood flow others believe that the vasodilating sympathetic nerves which emerge from the eighth cervical and first to sixth dorsal segments and are carried over the stellate ganglion represent the major factor The problem of the innervation of the coronary arteries is not yet fully solved

In addition to the aortic pressure and the tonus of the autonomic nerves (at times also the secretion of epinephrine by the adrenals) the coronary circulation is changed by (1) reflexes from various parts of the body and (2) by contraction of the myocardium in every phase of the cardiac cycle

REFLEXES Reflex changes of coronary blood flow play a very great role in coronary pathology but experimental data on this subject are scarce The

reason for this as pointed out before lies in the difficulty of demonstrating autonomic reflexes in experimental work To a high degree the different reflexes depend on the status of the receptors the nerve centers and the effector organs and these factors are altered through anesthesia Sufficient facts are known however to estimate the great part these reflexes play under certain circumstances

It is a common clinical observation that an attack of angina pectoris is experienced more often or exclusively after a heavy meal This occurrence is easily explained and will be discussed in one of the following sections Occasionally however the pain develops with the first few mouthfuls of food when the patient begins to swallow quite independently of the quantity and quality of the meal This event is explained by the diminution of the coronary blood flow after mechanical distention of the lower esophagus and stomach This vago vagal reflex disappears after the vagi are severed or after atropine is administered

There are a fair number of reliable observations regarding the appearance or aggregation of objective cardiac phenomena during gall bladder disease and their disappearance after the removal of the diseased viscus (Fitz Hugh and Wolferth)

Mechanical or chemical stimulation of the nasal mucosa decreases the coronary blood flow This is due to a reflex inhibition of the sympathetic vaso dilators (Gilbert et al)

Some physicians deny the existence of narrowing of the coronary arteries by nervous and humoral influences The coronary narrowing following an acute hemorrhage which will be discussed later and the marked narrowing following an intravenous injection of Pitressin show that this viewpoint is not justified

EFFECT OF SYSTOLE The phasic changes of blood flow during cardiac activity are a widely disputed topic Time and again it was assumed that coronary blood flow stops completely during systole while others conclude from their observations that the flow is enhanced by cardiac systole According to the studies of Wiggers and his co workers the phasic blood flow in the coronary arteries depends upon two factors (1) the pressure head in the aorta (2) the intramural tension The increased intramural pressure during the isometric period reduces the coronary blood flow but with the rise of systolic pressure in the ejection period the flow increases again The flow decreases again in *diastole* when the blood pressure is low There is a gradient of pressure from the outer layers of the myocardium to the subendocardial layers The latter are exposed to the high intraventricular pressure and the arteries are compressed during systole The outer layers of the myocardium are exposed to the negative pressure within the chest Increased heart rate reduces the coronary blood flow

Adaptation to Work Performed Under normal conditions the coronary blood flow is adapted to cardiac activity The arterial blood necessary for the heart for a given amount of work may be inadequate when the activity is increased It is not the absolute quantity of the coronary blood flow but the relation between the supply and demand that has primary importance

Increased work by the heart is accomplished in two ways (1) The minute volume may increase mainly by a greater stroke volume while the rate increases but slightly the return of blood to the heart is augmented so that diastolic filling and therefore the systolic output becomes greater (2) The same goal an increased minute volume can also be accomplished by a greater heart rate without marked changes of the stroke volume

The heart like any other engine consumes fuel (nutrient substances and oxygen) The paramount question from an economic standpoint is whether the relation between work performed and fuel consumption remains within a reasonable limit Investigations concerning oxygen consumption and cardiac blood supply during increased activity show that the heart muscle needs much less additional blood (oxygen) if it does the additional work by a larger stroke volume and a slow rate rather than by a small stroke volume and a fast rate Actually the heart of athletes during the training period adapts itself to a low rate and a larger stroke volume (Bainbridge) and therefore to the more economic type of heart action

These facts explain the clinical observation that even a slight increase of rate in certain cases of coronary disease has a detrimental effect If we possessed a remedy which could slow the heart rate and enable the heart to increase its activity only by greater filling we might obtain excellent therapeutic results in many instances of coronary disease

Epinephrine The importance of maintaining an increased blood supply when the demands are greater is well illustrated by the observation of the effect of epinephrine and atropine on the heart Epinephrine dilates the coronary arteries and increases the blood supply to the myocardium by as much as 50 per cent The increased rate the increased motility of the muscle and the higher metabolism following the administration of adrenaline however raise the oxygen requirement so much that myocardial ischemia may develop Even healthy young individuals with normal coronary circulation may experience anginal pain after the administration of only 1 ml of a 1 1000 solution (Raab) When the existence of coronary disease is suspected in a patient the administration of epinephrine in any amount is forbidden

Atropine Atropine also acts as a dilator of the coronary arteries by inhibiting the tonic vasoconstrictive action of the vagus It has been found that atropine more than amyl nitrite increases coronary blood flow (Rein) Atropine however usually increases the heart rate as well This leads to a greater demand for oxygen Accordingly patients in whom atherosclerosis precludes a dilatation of certain coronary branches or patients with syphilitic stenosis of the coronary ostia in which an increase of blood flow into the coronary arteries is likewise impossible may develop severe attacks of angina pectoris and very pronounced though transient changes in the electrocardiogram after the administration of a therapeutic dose of atropine (Scherf and Schnabel)

It is essential to note that neither an organic disease nor a reflex narrowing of the coronary arteries is the sole cause of ischemia and anginal pain The

failure to develop a necessary dilatation of the arteries in case of increased need for blood may be equally provocative

CARDIAC PAIN

The heart muscle as well as the epicardium seem to be insensitive to painful stimuli of chemical or mechanical origin Sensory fibers exist in the adventitia of the coronary arteries and veins and proceed over the Nervi cardiaci to the ganglion stellatum on the left side more than the right after leaving the sympathetic chain they enter the spinal cord with the white rami communicantes of the first to fifth dorsal segments The upper thoracic ganglia also receive direct sensory fibers from the heart There is no proof to show that pain fibers run in the vagus Cardiac pain is a true referred pain

Ischemia of the heart *muscle* itself does not seem to cause pain But pain may be produced by ischemia of the sensory nerve fibers running in the adventitia of the coronary vessels ischemia causes metabolites to accumulate locally just as in intermittent claudication

The sensitivity of different individuals to pain especially visceral pain varies to a great extent

Experiments in which the sensitivity of the nerve fibers in the adventitia of the coronary vessels was found high do not offer enough evidence to prove that ischemia is the real and only cause of pain in coronary disease Pain came after ligation and mechanical irritation of a coronary vessel (Singer Sutton and Lueth) Furthermore the instantaneous appearance of pain in all experiments speaks against the ischemic mechanism Ischemia can cause pain only after some time elapses and not instantly The experiments merely prove the existence of pain fibers in the adventitia of the coronary vessels

ANATOMIC CHANGES DUE TO ISCHEMIA

Ischemia of the heart muscle lasting longer than a few minutes results in necrosis of myocardial fibers particularly in the subendocardial layers around the papillary muscles and trabeculae (Buechner) Necrosis in this area appears in all conditions with a diminished oxygen supply to the heart muscle These necroses were mentioned earlier as a finding in pulmonary embolism They appear in carbon monoxide poisoning in shock and in advanced anemia particularly if the animal is forced to perform heavy physical work following an acute blood loss

Similar necroses in the myocardium have been found in patients who died after prolonged epileptic attacks and who showed normal coronary arteries Presumably they are not caused by coronary spasm but are due to the inability of the patient to breathe during the convulsions and the consequent hypoxia These necroses are also seen in attacks of angina pectoris of various types even with anatomically normal arteries (aortic stenosis) and of course in cases of coronary stenosis

ELECTROCARDIOGRAPHIC CHANGES DUE TO ISCHEMIA

The electrocardiographic changes caused by a moderate hypoxia of the heart muscle consist of a depression of the RS T segment and of the T waves in leads I and II and particularly in the chest leads (V4 V6) The RS T segment in aVF is elevated The same changes appear in the electrocardiogram if the area around the papillary muscle (which suffers at first in hypoxia of the myo cardium) is damaged mechanically (Boyd and Scherf) If more pronounced hypoxia exists in circumscribed areas of the myocardium the alterations in the electrocardiogram differ depending upon the site and extent of the ischemia

THE DIFFERENT CAUSES OF ANGINA PECTORIS

A disproportion between the blood supply to the heart muscle and the need for blood can occur

(1) In organic diseases of the coronary arteries Maximal ischemia appears in coronary occlusion and slighter grades in coronary diseases with stenosis

(2) In functional disturbances of the coronary arteries (spasm or failure of necessary widening in case of need) This disturbance appears in hypertensive crises in aortic valvular lesions pulmonary embolism and in acute hemorrhage

(3) In alterations of cardiac activity (increased cardiac work at the beginning of strenuous exercise paroxysmal tachycardias)

(4) Alterations of the blood (anemia carbon monoxide poisoning)

In the following sections these conditions which have one thing in common — a greater or lesser degree of myocardial anoxia — will be described in greater detail In all of these conditions pain may or may not appear

CORONARY OCCLUSION AND MYOCARDIAL INFARCTION

HISTORY

Knowledge of the great frequency of coronary occlusion is relatively old A series of excellent monographs was written on the pathologic aspect of this subject and complications such as cardiac aneurysm myomalacia and the like were elaborately discussed Some reports even showed the possibility of a clinical diagnosis of the lesion Most of these papers remained without noticeable influence on the thoughts of clinicians and sometimes even on the thinking of the very authors of the papers They continued to diagnose attacks of severe angina pectoris or status anginosus in patients who undoubtedly had a coronary occlusion Herrick however disappointed by the lack of response to his first papers continued to teach and publish on this subject Medicine is indebted to him for the fact that in the past thirty years coronary thrombosis has become one of the cardiac diseases that is diagnosed with a fair degree of accuracy

PATHOLOGY

Atherosclerosis and Thrombosis In the majority of cases coronary occlusion is due to atherosclerosis of the coronary arteries Other etiologic factors which are mentioned later represent rather rare exceptions In some cases the athero sclerotic process with atheroma formation fibrosis and lime salt deposits leads to a progressive stenosis and finally to a fibrotic occlusion of the vessels In one investigation no coronary occlusion existed in one third of the cases when the autopsy showed the existence of an infarction Only coronary sclerosis with narrowing of the lumen was found Added stress because of exertion paroxys mal tachycardia or increased output of adrenalin (Raab) may lead to an infarction in such subjects

In a greater number of cases the atherosclerotic process in the intima impedes endothelial nutrition and thrombosis of the artery occurs at this location Sometimes an atheromatous abscess opens into the lumen of the coronary artery and embolism or thrombosis develops

In a majority of cases however the occlusion is due to the rupture of giant capillaries in the wall of the atherosclerotic coronary arteries (Paterson) These giant capillaries arise in part directly from the lumen of the artery and in part from the adventitia (Wolkoff) They are numerous and due to their enor mous size and thin walls vulnerable If their wall ruptures and consequent hemorrhage occurs the intima above it may bulge into the lumen This occludes the artery Or the rupture may lead to damage of the endothelial lining so that thrombosis develops retrograde thrombosis from the ruptured capillary extending into the coronary artery from which it arises also occurs These mechanisms are certainly responsible for a vast number of occlusions in coronary thrombosis Nelson found this mechanism in 11 out of 17 instances and according to Horn et al it existed in 62 5 per cent of hearts with coronary thrombosis Snow et al frequently found recanalization in a thrombosed artery They found several infarctions following one occlusion Contrary to what others found these authors came to the conclusion that almost every coronary occlusion causes an infarction

Embolism Coronary occlusion is occasionally due to embolism Such cases *usually concern instances of acute or subacute bacterial endocarditis* during which small thrombi are detached from vegetations on the aortic or (more rarely) the mitral valves These cases are more frequent than one might suspect from reports since only a small percentage of them are published We had occasion to observe this occurrence twice in young women under twenty years of age who suffered from subacute bacterial endocarditis Sometimes emboli are due to detached mural thrombi or to fragments of atherosclerotic plaques

Following complicated fractures fat embolism of the coronary arteries is rather common and causes a variety of cardiac phenomena which are usually misinterpreted Even paradoxical embolism into the coronary arteries is known

Syphilis Syphilitic coronary occlusion involves only the orifice of the coronary arteries and is in reality an extension of the aortitis rather than an intrinsic disease of the coronary vessels Cases of myocardial infarction due to a syphilitic stenosis of the ostia have been described but usually the process evolves slowly and therefore causes a different clinical syndrome which will be described later

Other Lesions Coronary disease in periarteritis nodosa and in thromboangiitis obliterans is a rarity However these lesions as well as dissecting aneurysm may lead to an acute occlusion of a coronary artery and myocardial infarction Involvement of the coronary arteries in Takayashu s disease has been reported Myocardial infarction due to calcification of the coronary arteries in an infant (Traisman et al) and myocardial infarction due to serum sickness (Roussak) or sickling disease have been described

The coronary arteries may be invaded and occluded by primary or secondary neoplasms Examples of such metastases have been reported from many organs

Myocardial infarction has been observed following blunt trauma to the chest electric shock and barbiturate poisoning (Holzmann)

The atherosclerotic process occurs with equal frequency in all three branches of the coronary tree (right and left descending branches and the circumflex branch of the left coronary artery) This point must be stressed because for many years the descending branch of the left coronary artery was claimed to be the site of predilection

There are certain sites of predilection for occlusion within a branch such as the descending branch of the left coronary artery 1 cm after its origin

It is interesting that in cases examined pathologically usually at least two coronary artery branches show occlusion In many instances a new thrombosis developed in a patient who had an old occlusion of a vessel supplying the same area Sometimes occlusion occurs in all three large branches (Koch and Kong)

Necrosis of the myocardium (myocardial infarction) does not necessarily follow occlusion of a main artery This is especially true when the stenosis of a coronary artery progresses slowly and allows ample time for the collateral circulation to develop In these cases it may be possible to fill the whole coronary arterial tree by injection of contrast medium into only one artery The width of the anastomosing vessels may increase fivefold in such instances (Blumgart et al) Gradual occlusion of the coronary arteries in dogs also permits the development of a collateral circulation the latter is adequate to prevent the appearance of myocardial damage when this artery is completely closed

The activity of collateral vessels may reduce the infarction to an area much smaller than that supplied by the occluded vessel The infarction may be situated at some distance from the site of the occlusion In one instance myocardial infarction developed with all coronary arteries patent There was a marked fibrosis of the media which apparently led to a disturbance of function but the lumina of the coronary arteries were normal in width (Feyrter)

Healing A myocardial infarction heals gradually A reactive inflammation begins at its borders Connective tissue replaces the necrotic myocardial fibers and gradually a scar forms This process is completed slowly and requires some months The necrosis is fully developed after 4 to 6 days and fibrotic tissue appears in increasing amounts in the second week but the formation of collagen sometimes takes up to three months The scar becomes denser after three or more months Small infarctions heal after 5 weeks and larger ones after 2 to 4 months The size of the infarction its location the status of the coronary vascular tree and other factors may influence the speed of scar formation

Complications which may endanger the life of the patient will be discussed in the following pages

INCIDENCE AGE SEX

Incidence The incidence of coronary thrombosis in the general population is difficult to ascertain In many cases the diagnosis is not made in many attacks a physician is not called The disease is said to cause the death of 200 000 individuals yearly in the United States In a series of 1000 consecutive necropsies of all ages and both sexes myocardial infarction was found in 4 9 per cent For unknown reasons the incidence of the disease seems to be on the increase In recent years a seven fold increase of the number of cases has been reported (Morris) This is denied by others The disease is said to be rarer in the lower income groups The incidence of attacks has been found to be greater during the summer months The familial tendency is marked (40 per cent) (Bean) This is due in part to the frequent occurrence of hypertension in the same family

Blumgart found complete occlusion or marked narrowing of at least one and often of more coronary artery branches in 40 per cent of men over 40 years of age who died from a noncardiac disease

Age Since atherosclerosis of the coronary arteries occurs even in the newborn coronary occlusion with myocardial infarction may occur at any age Coronary thrombosis caused by acute rheumatic arteritis with myocarditis and endocarditis has been observed in an infant five months old In a 13 year old girl coronary occlusion with infarction led to the development of a cardiac aneurysm and rupture of the heart (Benda) Coronary thrombosis has also been observed in young men of 18 and 22 years respectively We observed myocardial infarction in a 21 year old girl This event is not remarkably uncommon in diabetics under 20 years of age

Sex Occlusion of a coronary artery is much more common in men than women the ratio being about 8 to 1 for younger individuals In old age as well as in hypertension and diabetes the incidence of coronary thrombosis is increased in women

OTHER FACTORS

Tobacco There is no proof that moderate smoking causes coronary sclerosis and thrombosis but the incidence seems to be greater in heavy smokers

Diabetes It was noted in a previous chapter that coronary sclerosis is typical of diabetes the same holds true for coronary thrombosis In diabetes coronary thrombosis appears not only more often but usually at an earlier age Among 274 cases in one series diabetes was found in 10 2 per cent (Conner and Holt) In another series of 300 cases diabetes was present in 17 4 per cent (Bean)

In individuals suffering from diabetes for only 5 years the incidence of coronary sclerosis seems to be increased It is believed by some that coronary sclerosis is not a complication of diabetes but an associated sign which appears even in carefully treated patients who scrupulously obey instructions concerning diet (Dolger) Others believe that full cooperation of the patient with regard to diet and insulin may diminish the incidence of vascular complications (Joslin)

Hypertension In hypertensives coronary sclerosis and coronary thrombosis occur much more often than in the general population Statistics dealing with the frequency of hypertension in patients with coronary thrombosis vary but estimates suggest that it is present in more than 50 per cent of the cases

Obesity Some authors deny that the incidence is greater in the obese (Vater et al) but the majority of investigators found obese patients in greater danger of developing the disease

Occupation Coronary thrombosis was found more often in people with sedentary occupations and it has been claimed to occur more frequently in physicians This has *not* been confirmed Actually Welsh miners were found to exhibit signs of coronary sclerosis in the same percentage as the general population

PRECIPITATING MECHANISM

In a majority of cases coronary thrombosis occurs without any apparent cause Attacks develop at rest often at night or during the customary daily work The occurrence of a thrombosis following trauma to the chest has been widely discussed and seems established *The outstanding part played by the rupture of the giant capillaries in the atherosclerotic intima in the development of coronary occlusion makes trauma and sudden strain possible factors* This question has extreme importance in legal medicine Occasionally coronary thrombosis occurs during *surgical shock or postoperatively caused by the fall of blood pressure* (Wasserman et al) A fatty meal shortens the clotting time and *may therefore precipitate an attack*

Myocardial infarction has been reported following poisoning with carbon monoxide Vigorous effort in a *patient with coronary sclerosis can provoke an attack* Fifty per cent of the fatal attacks in soldiers of the U S Army appeared during physical exertion *In such cases as pointed out above thrombosis is often absent* but the combination of coronary stenosis and effort caused the attack *of myocardial infarction* Fifty nine per cent of the hearts of these soldiers exhibited old myocardial scars

SYMPTOMS

Coronary occlusion and myocardial infarction are occasionally asymptomatic and are discovered accidentally In many cases there are however ample symptoms and signs to permit the diagnosis

Pain This is an outstanding symptom although figures about its incidence in myocardial infarction vary While previously believed to be the rule more recent observations show that pain is absent in 30 to 40 per cent of acute coronary occlusions (Boyd and Werblow) It has been mentioned that pathologists find at least one coronary artery occluded in the heart of patients who die with a simple angina on effort Not only a fresh occlusion but also an old one of another artery is discovered in those who die after they developed the syndrome of an acute myocardial infarction for the first time Slow fibrotic occlusion is more often less painful than acute thrombosis In some subjects this acute pain is absent but coronary occlusion is followed by angina on effort In other instances pain is intermittent The beginning of an infarction may antedate the onset of acute symptoms by days In psychotic patients 82 5 per cent of myocardial infarctions were painless that is patients did not complain of pain

The pain may be so severe as to develop into the most excruciating agony In most instances the pain — which may be viselike choking or burning — appears abruptly and in its full intensity There is no waxing and waning While temporary diminution and return to its original intensity occurs usually the pain is continuous It can be so savage that repeated injections of morphine may fail to relieve it Ordinarily the distress is felt behind the upper or middle section of the sternum and it may show typical radiation to the left or right arm to the neck or jaw and to the back between the shoulders Occasionally it radiates to the abdomen and it may spread to the left thigh this with other abdominal manifestations may convince the patient that he is suffering from a stomach disorder Sometimes the retrosternal pain is missing and the pain is felt only at the left elbow the ulnar side of the left (or right) arm or the left (or right) shoulder It is rare for the pain to last less than 30 minutes usually it remains for many hours and even days (status anginous) After it disappears there may be a residual soreness in the area for several days

The extreme severity of the pain may cause immediate syncope The concurrence of extreme anxiety and the severe pain often provoke great restlessness The patient is unable to sit still he moves around covers and uncovers himself alters his position or clutches at his clothing Complete immobility in an attack with severe pain is exceptional Severe sweating occurs

Between the two extremes — most severe pain and complete absence of pain — there are all transitional stages Pain may be tolerated quite well and the patient may continue work We have seen affected surgeons finish an operation despite distress Sometimes there is only pressure or soreness and the existence of pain is emphatically denied

The severity of pain allows no conclusion as to the size of the occluded vessel the extent of the infarction or the prognosis Even with the mildest distress indeed even with no discomfort a major branch of a coronary artery may be occluded As in other visceral diseases the violence of the referred pain shows great individual variation

Similar pains of equal duration of the same character and with the same radiation occur in other conditions and will be discussed later Nevertheless every pain of the type described however mild should arouse the suspicion of a coronary occlusion but such pain should never be the sole finding on which the diagnosis is based It is a serious mistake for the physician to overlook the diagnosis of a coronary occlusion merely because the prolonged pressure behind the sternum or in the epigastrium was not severe and amounted to mere discomfort But it is also a mistake to make the diagnosis simply because there was a severe pain in the left side of the chest which persisted for some time Prolongation of the pain or reappearance of it often means propagation of the thrombus and additional infarction

Dyspnea In most cases dyspnea is absent Its occasional occurrence was however described in early reports (Obrastzow and Strajesco) Even pulmonary edema is encountered Sometimes dyspnea is severe and the history of burning pain behind the sternum is elicited only by repeated questioning If sudden pulmonary edema develops in a patient without left ventricular hypertrophy and dilatation coronary occlusion should be suspected

Sometimes tachypnea is caused by apprehension or pain and may initiate the hyperventilation syndrome

If cardiac failure supervenes the types of dyspnea due to pulmonary congestion or cardiac asthma and Cheyne Stokes respiration may appear Hiccough is not rare and if prolonged represents a serious complication

Gastrointestinal Complaints Belching and even diarrhea are frequent symptoms Vomiting may be associated with nausea Frequent retching is often noted in patients who are unable to vomit The emesis is not caused by morphine alone it happens in patients who have not received this drug for the relief of pain or dyspnea It is explained by the activity of visceral reflexes originating in the heart muscle itself Severe meteorism may develop quickly this is particularly apt to occur when the blood pressure falls markedly and venous congestion appears

SIGNS

Physical examination of the heart often yields negative results

Percussion In many instances the heart is normal in size and shape This also applies to large and multiple infarctions and is somewhat astonishing in view of the extent and severity of the existing myocardial damage Absolute bed rest avoidance of heavy meals and fall of blood pressure lighten the load on the heart so that it can cope with its tasks despite almost mortal damage Under these conditions the destruction of a circumscribed area of the myocardium

could cause only a circumscribed dilatation (aneurysm) of the heart The heart is usually enlarged in patients in whom coronary occlusion complicates an existing hypertension

Auscultation This occasionally reveals loud and pure heart sounds In a majority of cases however the sounds soon are muffled, distant and indistinct The first heart sound may be very dull This phenomenon is particularly important if it develops during observation or in the hours or days following the onset of pain With progressive recovery and scar formation the sounds regain their loudness and become distinct This sequence provides a very valuable aid in checking the improvement of the cardiac status Sometimes months elapse before the heart sounds regain their original character In other cases the heart sounds are loud despite the development of large infarctions It has already been emphasized that in the presence of emphysema obesity or a markedly convex thorax distant heart sounds should not be regarded as pathologic Distant heart sounds are of importance only when normal heart sounds had been observed previously

In many patients particularly in those who develop a tachycardia the fact that both sounds are equally intense gives the impression of an embryo cardia Presystolic and — more commonly — protodiastolic and summation gallop rhythm develop Systolic murmurs may appear but more often they vanish if formerly present, because of cardiac weakness

Pericarditis An inflammation of the pericardium appears if the subepicardial layers of the myocardium are damaged (pericarditis epistenocardia) While pericarditis actually develops in a fairly large number of cases it is detected clinically in less than 20 per cent Although it is usually limited to the infarcted area sometimes it spreads over the entire heart At first nothing more than a soft systolic rub is heard usually at the apex and this is often confused with a systolic murmur later the typical tripartite friction rub appears Sometimes the friction rub may be audible only for a few hours in other cases it is easily detected for several days It is often missed because myocardial contractions are weak particularly in the infarcted area The friction rub may be audible as early as six hours after clinical evidence of coronary thrombosis is found or it may appear several days later In the second group one may assume a progressive coronary thrombosis and involvement of more branches so that the infarction extends to the outer layers of the myocardium which previously had escaped

In rare cases pericardial effusion accompanies the pericarditis This is recognized clinically on percussion by the temporary appearance of absolute flatness over the precordium a flatness of the same intensity does not develop from mere cardiac dilatation

The pericarditis in general represents a desirable complication for the local inflammation speeds the healing process The local adhesions which develop as an aftermath increase the strength of the developing scar and may prevent rupture of the heart In many cases at necropsy the myocardium in the area of

pericardial adhesions is as thin as paper and is translucent In one observation a hole over 1 cm in diameter was found through a partial aneurysm covered by a pericardial adhesion (Scherf and Erlsbacher) Histologic examination of this section revealed no myocardial fibers at all In this instance a perforation of the ventricle was closed by the pericardial adhesion and life was prolonged for a time

Fever Elevation of the temperature has great diagnostic importance It is one of the more constant signs of coronary thrombosis Usually it appears after a lapse of fifteen to twenty hours but sometimes not for two to three days The height of the temperature varies In one patient it may be slight (37 2 C) in another it may reach 41°C In the absence of complications it subsides by lysis after persisting four to seven days In some cases a slight elevation exists only for a few hours but we have seen fever persist for many weeks with no demonstrable cause In some of these patients a large infarction exists with pericarditis and pneumonitis

Congestive heart failure pulmonary edema or pulmonary infarction cause sudden increase or reappearance of fever Additional extension thrombosis or late appearance of pericarditis have the same effect

The increased temperature in cases without complications is said to depend less on the reactive inflammation developing in the area surrounding the necrotic section of myocardium or on the pericarditis than in the absorption of abnormal protein products from the necrotic infarcted area Fever occurs in the absence of pericarditis and often too soon for a reactive inflammation Accordingly the elevation of temperature is equivalent to the fever developing elsewhere in connection with necrotic processes Its relatively early appearance may be explained by the fact that cardiac contractions continuously expel abnormal substances from the necrotic myocardium into the circulation There is no explanation available for the fast disappearance of the fever

Occasionally elevation of temperature is absent In one series of cases an increased temperature appeared in only 66 per cent (Baer and Frankel) In our experience the incidence is higher

Blood Pressure The fall of blood pressure constitutes one of the most important signs of myocardial infarction During the attack of pain and in the early hours after the attack begins the blood pressure is often high occasionally it is even impressively higher than it was prior to the attack (Scherf) However it soon starts to fall more or less rapidly This phenomenon represents a very valuable diagnostic sign of myocardial infarction

The rapidity and extent of the fall are variable and have great prognostic significance In some cases the drop is immediate and shock appears Shock is diagnosed by many clinicians when the blood pressure is 90 mm Hg or less and the pulse pressure is 20 mm Hg or less On the other hand one sees patients with a systolic blood pressure of 80 mm Hg and a pulse pressure of 15 mm Hg persisting for weeks without any manifestation of shock Often even in the absence of shock the fall may amount to 100 mm Hg — for example the systolic

pressure may fall from 220 to 100 mm Hg In other cases the slow decline continues for several days and may not exceed 30 mm Hg or the blood pressure may remain unchanged If levels as low as 70 or 80 mm Hg are reached the situation becomes critical for the blood supply to the vital centers may suffer In individuals with sclerotic arteries even a moderate fall of blood pressure may appreciably reduce the blood supply to such vital organs as the cerebrum or kidneys Loss of consciousness incontinence of urine and stool facial or limb paralysis or anuria may appear — without evidence of shock — and vanish if the blood pressure again rises A fall of blood pressure may be lethal *per se*

The diastolic blood pressure also falls though less than the systolic There fore the pulse pressure may diminish significantly

The lowered blood pressure may rise within a few hours days weeks months or even years and regain its previous level Often however it remains at a decidedly lower level despite the fact that the patient feels well shows no signs of decompensation and pursues his occupation normally This observation in particular makes it difficult to explain the fall in blood pressure by myocardial damage alone The fall is usually not due to shock for in a majority of cases it is found without severe pain or shock Experimentally a fall of blood pressure appears quickly after ligation of the descending anterior coronary artery but the resulting localized myocardial damage is soon compensated by an increased diastolic size of the heart and the blood pressure regains its normal value Occasionally there is even some overcompensation and a rise of pressure There is some experimental evidence for a reflex fall of blood pressure following myo cardial damage the vagus representing the afferent path (Bezold Jarisch reflex) Further work on this important problem is needed

The marked decline of blood pressure may be accompanied by a desirable lassitude and sleepiness which make it easier to keep the patient quiet Another advantage of the lowered blood pressure provided it remains within certain limits is the reduction of strain on the severely damaged myocardium Un doubtedly many patients would not survive a large cardiac infarction were it not for the reduction of blood pressure

Urine Not uncommonly the examination of the urine discloses a slight albuminuria and glycosuria (Levine) In 100 cases investigated personally glycosuria appeared in 10 per cent The amount of urinary sugar may reach 1 per cent and acetonuria is often present The glycosuria is accompanied by hyperglycemia (Scherf) and the fasting blood sugar may exceed 300 mg per cent Originally explained by shock by renal damage or by a coexisting sclerosis of the pancreatic arteries it was later attributed to the activity of reflexes regulating blood pressure (Scherf) As in other stress situations the work of the adrenal cortex was found increased This is proved by the disappearance of eosinophiles from the circulating blood an increased secretion of catechols speaks for a greater function of the adrenal medulla (Raab) The 17 ketosteroids in the urine are increased There is also a distinct creatinuria The reflexes proceed over the carotid sinus and increase the output of norepinephrine whose

effect in elevating the blood pressure is generally known In addition fever hypoxia hypercapnia and drugs (morphine and caffeine) which are frequently given to these patients may increase the blood sugar level Hyperglycemia and glycosuria appear in the absence of shock or even pain

The glycosuria and hyperglycemia are transient and usually vanish within a few days In many patients all signs of a disturbed carbohydrate metabolism are absent if examinations including the sugar tolerance curve are made after a few days

If coronary occlusion occurs in a diabetic individual extremely careful observation is necessary since a previously mild diabetic may sink rapidly into coma

In impending coma occasionally severe pain appears in the upper abdomen and the differential diagnosis between diabetic coma without complication or coma in a case of coronary occlusion will be difficult

Nonprotein Nitrogen About one third of the patients with myocardial infarction have an elevation of the nonprotein nitrogen content in the blood This may be due to the anuria in patients with shock In other instances reduced kidney function associated with atherosclerosis of the renal vessels and the fall of blood pressure is the initiating factor A similar increase of the nonprotein nitrogen in the blood may appear in heart failure It is temporary if the patient recovers

Leukocytosis This occurs in most cases of coronary thrombosis It may be found shortly after the beginning of the symptoms and the count may reach 30 000 per cubic millimeter there is relative and absolute increase of the polymorphonuclear cells and a drop in eosinophiles It occurs before or during the fever and often lasts only for one or two days A second rise appears if other vascular occlusions occur in the peripheral arteries or in the lungs If the white blood cell count surpasses 25 000 the mortality is said to be about 100 per cent The eosinophiles reappear within 5 to 7 days Occasionally lymphocytopenia has been reported in acute infarction (Altschul)

Sedimentation Rate of the Red Blood Cells Coagulation Test Increased sedimentation rate has had great significance in the recognition and management of myocardial infarction ever since its frequent occurrence in these cases was realized The increase may not be detected until the fourth or sixth day after the occlusion but values exceeding 100 mm in one hour (Westergren method) are observed The importance of this finding lies in the fact that these abnormal values may persist for weeks after the infarction that is they may be present at a time when other clinical signs such as fever blood pressure changes and leukocytosis have long since disappeared

Acceleration of the sedimentation rate of the red blood cells is without doubt an extremely ambiguous phenomenon that should not be evaluated alone In many cases where the suspicion of a myocardial infarction exists however this finding without another satisfactory cause supports the diagnosis particularly if the values rise a few days after the attack

The cause of the accelerated sedimentation rate seems to be the absorption of protein products from the necrotic heart muscle As a matter of fact the sedimentation rate is increased approximately as long as the healing process in the necrotic portion of the myocardium is incomplete For this reason determinations of the sedimentation rate are extremely valuable in appraising the progress of the restorative process The increase of the rate roughly parallels the severity of the lesion In small infarctions the rate remains normal

Occasionally abnormal values are obtained even six to eight weeks after the infarction In these patients if no other cause (latent infection anemia) is present bed rest may have to be prolonged In a majority of cases normal values are obtained within four to six weeks In rare instances the sedimentation rate remains high for many months for no apparent reason In these cases one should proceed cautiously and permit the patient to be up and about if the clinical findings are satisfactory

The sero coagulation band of Weltman has been found a valuable substitute for the sedimentation rate in myocardial infarction

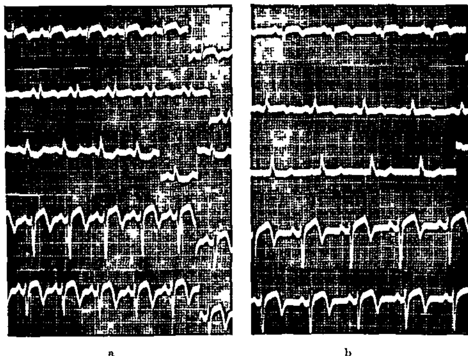
Transaminase Test The serum glutamic and oxalacetic acid transaminase (SGO T) test which seems to be of great value has been developed by La Due and Wroblewski This test is based on the fact that a tissue enzyme glutamic oxalacetic transaminase has its greatest concentration in the heart muscle The normal transaminase has a range of between 10 and 40 units The average peak in myocardial infarction is 164 units per ml (Ostrow et al) but much greater values are obtained This serum activity of transaminase is not increased by infections degenerative neoplastic or other states unless there is acute damage of the heart or skeletal muscle liver or kidney The authors worked out a relatively simple spectrophotometric test of the transaminase (aminopherase) False negative tests are rare Pathologic values are those over 48 units per ml If only one test is performed it is best to do it 24 hours after the beginning of the attack Otherwise it is preferable to perform one test about 6 hours after the onset of symptoms and a second test after 24 hours The transaminase blood levels are normal again five days after the attack The highest values were seen in patients with hemorrhagic pancreatitis (over 16 500 units)

Pulmonary infarcts may also cause abnormal tests Abnormal values are also observed in myositis In patients with bundle branch block where the electrocardiogram so often does not show the characteristic patterns the test often is of great value

Other enzymes (aldolase dehydrogenase malic acid dehydrogenase) are also increased in the blood (Siegel et al)

Other Findings Kroop and Shackman found the C reactive protein test positive in patients with myocardial infarction Wilhelm found changes in the electrolyte pattern Feldthusen and Lassen described a diminished serum iron (hypoferriaemia) after coronary occlusion and cardiac trauma Serum zinc levels are lowered after myocardial infarction (Wacker et al)

X ray Examination This has limited value since it is necessary for the patient to remain in bed for several weeks An elevated position of the left diaphragm has been described (Borak) it appears in the early stages and may be due to the left sided pleurisy following pericarditis Abnormal excursions and absence of pulsation along the left cardiac border have been described in connection with fluoroscopy and kymography but these findings have only limited value and cannot be used for diagnosis Due to the multiplicity of cardiac



a b

FIG 62 (a) Typical tracing of an antero lateral wall infarction obtained during th acute clinical picture in a 48 year old man There is a low QRS complex in lead 1 with a comparatively deep Q wave The RS T segment is elevated in lead I and depressed in lead III The R waves are low in V 5 there is a peaked deeply inverted T wave in V 2 and V 5 preceded by an elevated RS T segment Nine days later figure 62b was obtained There is a wide slurred Q in lead I followed by a deeply inverted T wave there is little change in the chest leads

movements with every systole shortening along the axis widening of some parts in the transverse diameter and rotation pulsations may be absent normally in local sections of the left cardiac border (Zdansky)

Electrocardiogram The electrocardiogram possesses primary importance in the establishment of the objective diagnosis of coronary occlusion

Experimental observations show that the alterations in the electrocardiogram may appear within 40 to 60 seconds after ligation of a coronary artery Clinically

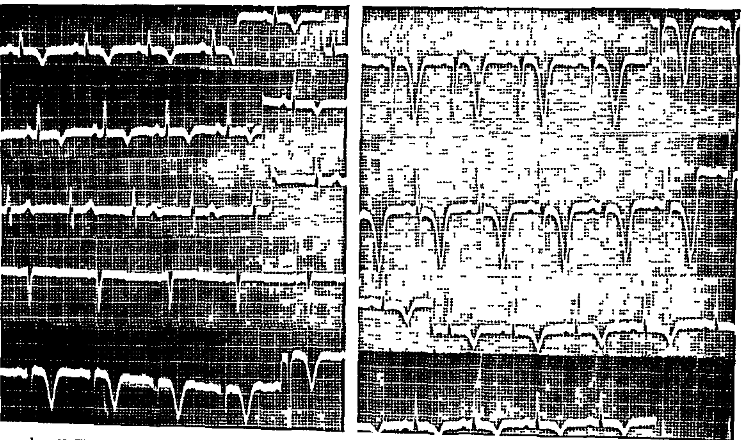


FIG 63 This figure reproduces the standard leads and the six chest leads of a 46 year old woman with an acute myocardial infarction With the exception of the absence of an R wave in V 3 there are no changes of the QRS complexes The T waves are deeply inverted peaked and symmetrical in all leads with the exception of leads III and V 1

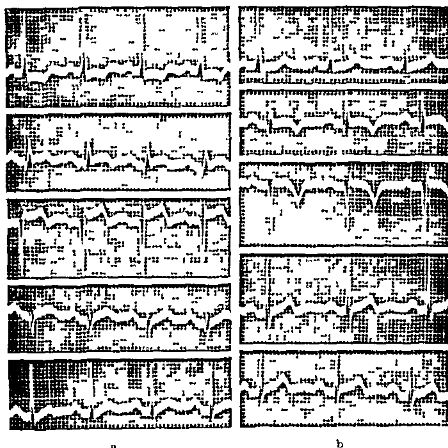


Fig 64 (a) The pattern of an inferior wall infarction 20 hours after the beginning of the attack figure 64b was obtained 22 days later

Figs 65–6 see pages 406 and 407

Fig 65 This electrocardiogram was obtained from a 3 year old woman suffering from an acute inferior wall myocardial infarction There is an atrial tachycardia with 2 1 block The P R interval is prolonged to 0 24 second The depression of the RS T segment in lead I and the elevation in lead III are clearly seen In V 2 V 6 there is a depression of the RS T segments which is typical for the acute stage of an inferior wall infarction

Fig 66 This is the electrocardiogram of a 56 year old man with clinical signs of an acute myocardial infarction The standard leads show only abnormal T waves there are however abnormal QRS complexes (no R waves) in lead V 2 and V 3 and a typical elevation of the RS T segment followed by an inversion of T waves in lead V 3 and V 4 These changes speak in favor of an involvement mainly of the anterior wall of the left ventricle

Fig 67 This electrocardiogram was obtained from a 58 year old patient who experienced his second attack of myocardial infarction Lead I shows a low QRS complex with a relatively deep Q wave in leads II and III broad Q waves are present a typical elevation of the RS T segments is seen in leads V 3 V 5 An acute anterior wall infarction was superimposed on an old inferior wall infarction

FIG 65

FIG 66

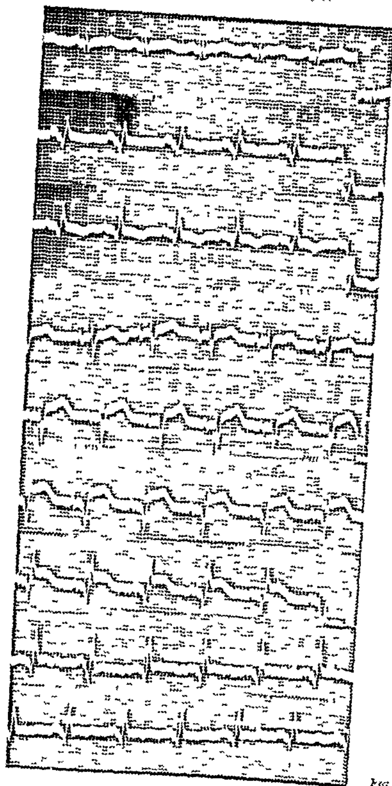


Fig 67

these alterations sometimes last for weeks or months in fact the electrocardiogram may remain abnormal throughout the patient s lifetime

In many cases the changes are characteristic and permit the localization of the infarction Certain patterns indicate an infarction of the antero lateral area or of the anterior wall of the left ventricle due to an occlusion of the descending branch of the left coronary artery other patterns indicate an infarction of the inferior or posterior part of the left ventricle due to an occlusion of the posterior descending branch of the right coronary artery

In figure 62a the typical tracing of an acute infarction of the antero lateral wall of the left ventricle near the apex is reproduced The tracing was obtained from a 48 year old man who had suffered from severe pain behind the sternum for 12 hours when the electrocardiogram was taken The tracings show the typical pattern There is a high take off of the RS T segment from the descending branch of the P wave in lead I and a low take off in lead III A very pronounced inversion of the T waves is present in the chest leads (V 2 and V 5)

Figure 62b shows the electrocardiogram of the same patient nine days later It reveals the typical evolution in the standard leads while the chest leads are almost unchanged

Figure 63 shows the electrocardiogram of a 46 year old woman who suffered from an acute infarction 12 days previously There is a deep inversion of the T waves in leads I and II as well as in most chest leads

In figure 64 a and b the typical early and late pattern of an inferior wall infarction are reproduced The tracings were obtained from a 59 year old woman The electrocardiogram of figure 64a was taken 20 hours after the beginning of pain due to myocardial infarction figure 64b was taken 22 days later

In figure 64a there is a depression of the RS T segment and an inverted T wave in lead I There is a deep Q wave and a high take off in lead III The chest leads (CR 2 and CR 4) show no changes Figure 64b shows the typical evolution with a return of lead I to normal and the deep abnormal Q waves with inverted T waves in leads II and III

Figure 65 shows the acute stage of an inferior wall infarction with 2 1 block and a prolongation of the P R interval while figure 66 shows the pattern of an infarction of the anterior wall of the left ventricle In figure 67 an acute anterior wall infarction was superimposed on an old inferior wall infarction

For a more detailed discussion of these and other patterns seen in myocardial infarction we refer the reader to our book on electrocardiography

Frequently other changes such as bundle branch block appear in the electrocardiogram but they are not characteristic Occasionally alterations are absent for days and sometimes they are missed despite many examinations Repeated tracings particularly of the six chest leads are necessary if the first records are normal

In small infarctions situated supra apically or only in the inner layers of the myocardium no changes in the QRS complex are seen and only T wave

alterations appear (figure 68a) Figure 68b was obtained 3 days later and shows a marked tendency to normalization Four days later a very pronounced inversion of the T waves is visible (figure 68c) The patient a 56 year old woman experienced pain only at admission to the hospital A propagation of the thrombus is a possible explanation for the deterioration in figure 68c However one sees in infarctions temporary normalization in the electrocardiogram (as in figure 68b) for other reasons e g an accompanying pericarditis

No conclusion is permitted with regard to the size of the infarction as is often claimed from the degree of alterations It can be shown that minute

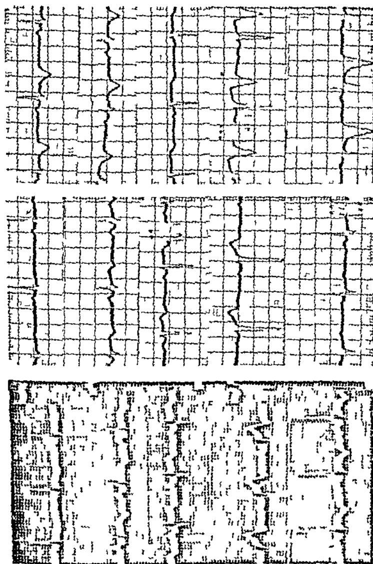


Fig 68 A 56 year old woman was admitted with clinical evidence of an acute myocardial infarction The first electrocardiogram (a) shows the changes seen in left ventricular hypertrophy and also in certain infarctions involving the inner myocardial layers The tracing obtained three days later (b) shows a tendency toward normalization (c) Changes which suggest an anterolateral wall infarction obtained 4 days after (b)

damage of the superficial layers of the myocardium in certain areas where infarctions occur typically (apex or base of the left ventricle) cause marked changes while damage of the deeper layers of the myocardium or damage of areas not in contact with the diaphragm or the long dorsal muscles in front of the spinal column cause slight or noncharacteristic alterations The extent of the alterations therefore does not give any indication about the size of the infarcted areas

Since the electrocardiogram may be markedly altered in small infarctions at special locations and may show no or only slight changes in large infarctions at other sites no conclusion as to the prognosis or the management is permitted from the electrocardiogram

In cases with bundle branch block or with old previous infarctions or even with a marked hypertrophy pattern typical changes are often missed

COMPLICATIONS

In acute myocardial infarction cardiac output falls the cardiac rate increases venous pressure often rises and the peripheral resistance increases presumably due to the output of large quantities of pressor amines as a compensatory measure

In the period immediately following coronary thrombosis certain complications may arise some endangering the life of the patient Some are partly or wholly preventable and others demand emergency treatment An awareness of these complications is indispensable

Cardiac Arrhythmias These are not uncommon after coronary occlusion and often they represent very serious complications Some observers noted them in 48 per cent of cases (Rosenbaum and Levine) Disturbances of stimulus formation are usually responsible

As early as 1881 Cohnheim reported that ligation of a coronary artery may induce cardiac arrhythmias within 30 to 40 seconds and may lead to the condition now known as ventricular fibrillation The importance of these observations for the explanation of sudden death of patients with coronary diseases was stressed by this observer

Subsequently these arrhythmias were restudied with the aid of the electrocardiogram on dogs and monkeys with the same result Following the ligation of a main branch of the coronary arterial tree extrasystoles may appear within a few minutes Sometimes hours or (rarely) even days elapse before they develop The extrasystoles are most commonly of ventricular origin but occasionally they originate in the atria Extrasystoles appear particularly after an occlusion of the right coronary artery The extrasystoles are often multiform indicating their origin from different foci attacks of ventricular paroxysmal tachycardia appear and ventricular fibrillation suddenly develops At other times ventricular fibrillation appears suddenly without preliminary extrasystoles In one series of 50 experiments on dogs ventricular fibrillation appeared in 15 animals (Harris and Hussey) In another series on monkeys ventricular fibrillation occurred in 10 of 32 experiments when the right or left descending coronary artery was

ligated. The first forty minutes are the most dangerous because fatal fibrillation occurs most often during this period. Ventricular fibrillation has been registered electrocardiographically during attacks in man and there is good reason for assuming that sudden death in patients with coronary disease is due to this mechanism. Ventricular extrasystoles and paroxysmal ventricular tachycardias are not rare in patients with myocardial infarctions.

Figure 69 shows the three standard leads of a 42 year old man admitted to the hospital because of severe chest pain. Despite the presence of slurring and

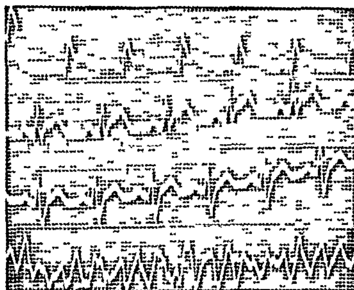


FIG 69. Acute antero lateral wall infarction with bundle branch block. Ventricular fibrillation appeared while the electrocardiogram was recorded (lowermost tracing, lead V 2).

widening of the QRS complexes, the elevation of the RS T segment characteristic for antero lateral wall infarction is visible in leads I and II. While the technician switched from lead III to lead V 2 the patient lost consciousness and ventricular fibrillation was registered.

While ventricular fibrillation need not necessarily follow single extrasystoles and while experimental ventricular fibrillation may develop without preliminary extrasystoles, the presence of extrasystoles shows that the patient is in danger. These arrhythmias always represent a serious finding and require immediate treatment.

Among 92 patients with acute myocardial infarction 20 had extrasystole and of these 8 died (Padilla and Cossio). All four patients with multiform extrasystoles succumbed. Fourteen out of 17 patients who developed frequent ventricular extrasystoles following myocardial infarction died (Woods and Barnes). Other observers believe that the appearance of extrasystoles does not alter the prognosis materially. It is important to realize that the sequence of

extrasystoles paroxysmal tachycardia and ventricular fibrillation may appear in a few minutes and is usually not observed by the physician The authors are in complete accord with those who consider the appearance of extrasystoles after a myocardial infarction a serious complication

During asphyxia of the entire heart extrasystoles do not appear probably because there is diminished excitability of the entire myocardium

In experiments on dogs prophylactic treatment with quinidine has been found relatively ineffective In man however with the appearance of extra systoles and *to a greater extent of paroxysmal tachycardia* immediate administration of quinidine is very helpful It is claimed that the routine practice of giving daily doses of quinidine in a large hospital to all patients in danger of developing ventricular fibrillation reduced the number of sudden deaths remarkably Apart from the danger of ventricular fibrillation the damage produced in these hearts by paroxysmal tachycardia with a rapid rate per se is so great that it requires the immediate use of *quinidine* Even if large doses of quinidine are necessary the danger from it is less than that from a persistent tachycardia This question will be further discussed later in this chapter

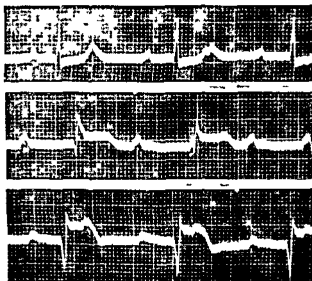


FIG 70 *Complete heart block in a patient with an acute inferior wall myocardial infarction*

Sometimes atrial fibrillation and flutter appear In the first condition immediate digitalization is indicated to slow the rate The latter disturbance is usually treated with quinidine but digitalis is preferred by many We often use strophanthin

It was pointed out earlier that the sinus node usually obtains its blood from the right coronary artery If the right coronary artery is occluded close to its orifice disturbances of stimulus formation in the sinus node such as sinus bradycardia or sinus arrhythmia may develop These bradycardias are beneficial because of the greater efficiency of the heart with slow rates We have seen congestive failure and gallop rhythm develop immediately after this bradycardia vanished

Since the A V node and the bundle of His are also supplied from a branch of the right coronary artery in most cases partial or even complete heart block is not rare when this artery is occluded and inferior wall infarction appears

Figure 70 shows an electrocardiogram taken from a 69 year old woman with the clinical picture of myocardial infarction There is a typical pattern of a fresh inferior wall infarction with complete atrioventricular block Atria and ventricles contract regularly but independently of each other

A partial heart block in a patient with inferior infarction is seen in figure 71 The atrioventricular rhythm in figure 72 is in all probability caused by non function of the sinus node due to the occlusion of the right coronary artery near

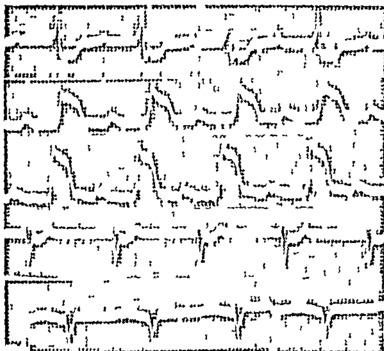


FIG 1 In a 51 year old man with the clinical signs of an acute myocardial infarction the conduction time is prolonged to 0 40 second and 2 1 block exists there is marked elevation of the RS T segment in leads II and III indicating an acute inferior wall infarction The chest leads (V 2 and V 5) show signs of an old antero lateral infarction

its orifice Auricular flutter in a patient with anterior wall infarction is seen in figure 73

All types of partial A V block and complete heart block may appear and Stokes Adams attacks may occur Sometimes the heart block vanishes in a few hours or days Under these circumstances as mentioned above the condition of the patient may change for the worse as the rate increases and sinus rhythm returns

Shock A very serious complication of coronary thrombosis with myocardial infarction is the appearance of peripheral circulatory failure or shock The cause is not clear The fall of the cardiac output or the overwhelming pain may

be responsible in some patients in other patients the appearance of arrhythmias with too rapid or too slow rates and in still other patients reflexes of the type of the Bezold-Jarisch variety may be responsible Thus central (cardiac) and peripheral mechanisms may be determining factors

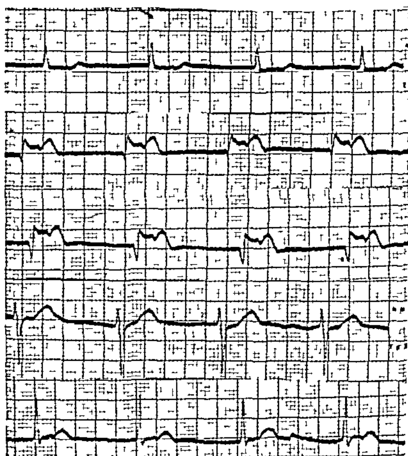


FIG 72 In a 72 year old woman with clinical signs of an acute myocardial infarction the electrocardiogram shows the pattern of an inferior wall infarction There is a bradycardia of 60 beats per minute and the sinus rhythm is replaced by an atrioventricular rhythm with a P wave (inverted in leads II and III) between the QRS and T waves

Opinions regarding its incidence vary Some believe shock occurs in 10 per cent of all myocardial infarctions while others consider it to be more rare Such diversity of opinion derives from the arbitrary method of diagnosing light shock Some physicians consider all patients to be in shock whenever the blood pressure is 90 or less while others diagnose shock whenever the pulse pressure is 20 mm Hg or less It is a good practical rule to watch the patient carefully and supervise him as constantly as one would a patient in diabetic coma as soon as the systolic blood pressure falls to values around 100 and the pulse pressure threatens to reach values around 20 In our opinion there are patients in shock

with higher blood pressure values while others have for weeks a systolic blood pressure of 80 and a pulse pressure of 20 without being in shock It is in the latter group of patients in particular that early energetic therapy may do more harm than good

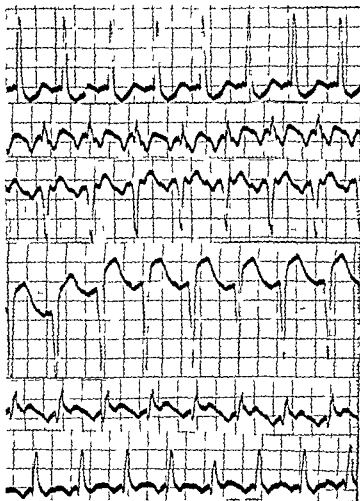


FIG 53 Atrial flutter with 2 1 block and signs of an acute anterior wall infarction (lead V 3) in a woman 78 years old

Shock should be diagnosed by other clinical signs — sinus tachycardia ashen grey color cold perspiration weakness and anuria

The mortality is markedly increased by the appearance of this complication It seems to amount to 80 to 90 per cent if severe shock is present Temporary fall of the blood and pulse pressure does occur but it is often compensated after a short time by regulatory mechanisms Even overcompensation with a rise of blood pressure may be observed (Orias) During shock the danger of

intravascular thrombosis (cardiac cerebral mesenteric) is great It may be followed by the development of lower nephron nephrosis

The early diagnosis is of importance since statistics indicate that therapy initiated when the shock has lasted more than 3 hours is of very dubious value

Perforation of the Ventricular Wall and Cardiac Tamponade Originally this event was described by Harvey Perforation of the ventricular wall in the infarcted area usually occurs in the first two weeks In one series the earliest appearance was 14 hours after the onset of symptoms and the latest was on the sixteenth day (Bean) Among 7000 autopsies spontaneous rupture of the heart was observed 40 times (0 57 per cent) (Benson et al) In another series of 25 000 necropsies cardiac rupture was seen 72 times (Edmondson and Hoxie) This tragic complication occurs in 2 to 4 per cent of myocardial infarctions Often there is no hole in the muscle but the blood oozes slowly from the infarcted area separating the layers of myocardium and cutting a tortuous path from endocardium to epicardium Rupture occurs very rarely through an old scar Many of these cases are encountered by medical examiners since the coronary occlusion preceding the cardiac rupture often remains unrecognized and the patient dies suddenly Rupture usually takes place on the anterior wall of the left ventricle above the apex The decisive factors are the amount of softening and the height of the blood pressure Rupture seems more common when hypertension persists

Rupture of the ventricular wall is usually immediately fatal Exceptions like the case mentioned above where an adherent pericardium covered the opening created by the perforation are rare

Rarely patients survive the oozing of blood and cardiac tamponade The latter is generally treated conservatively (aspiration) but surgery with suture of the involved area should be considered more often

Perforation of the Interventricular Septum This complication causes a typical clinical syndrome with the sudden appearance of a thrill and a loud systolic murmur over the fourth and fifth interspaces to the left of the sternum The heart undergoes marked dilatation and evidence of congestive failure soon appears

The patient may survive this complication for years One case was observed for four years and ten months with a perforated interventricular septum following coronary thrombosis while one of us had a similar patient under observation for three and one half years

Rupture of a papillary muscle of the left ventricle causes a loud whistling to an fro murmur that is often high pitched Sometimes there are no murmurs The clinical diagnosis is difficult Patients rarely survive more than a few hours

Postmyocardial Infarction Syndrome Dressler describes a postinfarction syndrome resembling idiopathic pericarditis Despite absence of hemorrhagic sputum in these patients we believe that the combination of pericarditis with pleurisy and pneumonitis could be explained by pulmonary infarctions Post

mortem examinations will certainly decide the issue in the future According to the author cortisone is the preferred therapy

Abscess Formation This is a rare complication in the infarcted area It appears also in sepsis pneumonia and pyelitis

Dyspnea This is a common and serious complication Often it is paroxysmal and in coronary thrombosis pulmonary edema may be the equivalent of an attack of pain Paroxysmal dyspnea and pulmonary edema may develop at any time after an infarction but they are prone to appear in the first two weeks If pulmonary congestion predominates there is continuous dyspnea and orthopnea

Moist and dry rales over the lungs for the most part at the bases are common The dyspnea is rapidly controlled by morphine which must be given day and night in these cases to afford relief Moist rales over the bases of the right and left lung are extremely common and bear continuous watching The advisability of digitalis therapy if pulmonary congestion and right heart failure supervene will be discussed later

Pulmonary Effusion Left pleural effusion is not unusual and is due to irritation of the pleura following the pericarditis A left sided pleural effusion of obscure origin in a man over forty years of age should always arouse the suspicion of a myocardial infarction Too often the infarction is overlooked and the patient is treated symptomatically for the pleural effusion

Peripheral Vein Thrombosis and Pulmonary Embolism This is a very common complication and everything possible must be done to prevent it The impairment of circulation is one of the more frequent causes of venous thrombosis all statistics dealing with the incidence of fatal pulmonary embolism stress that most of these cases concern those affected with a cardiovascular disease In patients with myocardial infarction the combination of a marked fall of blood pressure and enforced prolonged rest in bed is a typical and regular cause of thrombosis in the pelvic veins this is the usual source of pulmonary emboli Such emboli may occur as early as 10 to 15 hours after the onset of symptoms

The discussion of the effects of pulmonary emboli on the heart and circulation in a previous chapter should make it clear that this additional new burden for the severely damaged heart creates serious problems and often causes early death

The diagnosis many times is missed the symptoms or signs being attributed to a new myocardial infarction The differential diagnosis between the two conditions as well as prophylactic measures will be discussed below

Statistics about the incidence of thromboembolic phenomena in patients with myocardial infarction give figures varying from 5 to 33 per cent

Peripheral Embolism This is produced by mural thrombi from the left ventricle Since the inner layers of the myocardium are often involved in cardiac infarction endothelial damage leads to the formation of thrombi These thrombi are found in almost 50 per cent of fatal myocardial infarctions and have been noted as early as 24 hours after the onset of coronary occlusion With healing slow fibrosis occurs and only a slight thickening of the endocardium remains

Occasionally there are lime salt deposits which may be visualized by x ray In some cases on the other hand the thrombus liquifies and becomes fragmented and multiple peripheral emboli develop Despite the high incidence of mural thrombosis peripheral embolism fortunately is not very common

Embolism of the cerebral arteries causes hemiplegia and other forms of paralysis The spleen kidneys or mesentery are also frequent sites of embolism Sometimes the thrombus fragments into multiple emboli which lodge in the viscera and extremities Occlusion of a leg artery may necessitate embolectomy or amputation

Mural thrombi also occur in the right ventricle an event which usually happens when the right side of the interventricular septum is affected These thrombi may be the source of pulmonary emboli

The sudden marked fall of blood pressure in patients with severe atherosclerosis of the cerebral and peripheral vessels may lead to the formation of arterial thrombi and may cause syndromes similar to those of embolism Differential diagnosis is often impossible

If the myocardial infarction causes no symptoms the only evidence of a cardiac lesion may be one of the embolic syndromes just mentioned Embolism seems to occur often when the heart is not severely damaged by the infarction and still contracts vigorously Peripheral embolism is observed as early as 24 hours after the occlusion or as late as many weeks after

Neurologic Signs Confusion attacks of unconsciousness and epileptiform convulsions occur even in the absence of heart block or tachycardia Temporary paralysis of an extremity or the facial muscles may appear

Jaundice and Hemoptysis These are not uncommon early complications that often follow pulmonary embolism with infarction Hemoptysis occurs at times in the first 24 hours Thrombosis or embolism of a pulmonary artery or a reflex vascular spasm in the lesser circuit contribute to the development of these accidents

Cardiac Aneurysm For centuries marked dilatation of a cardiac chamber has been called an aneurysm Thus even in recent times the term has been applied to the great dilatation of the left atrium in mitral stenosis At present however the term cardiac aneurysm or partial cardiac aneurysm is reserved for a bulging of a portion of the wall of one cardiac chamber Usually the wall has undergone marked change A cardiac aneurysm may be due to trauma syphilitic gumma large tubercle trypanosomiasis (Mora et al) developmental anomalies (Martin) severe focal myocarditis (even in rheumatic fever) or a mycotic abscess but as a rule it is the result of coronary occlusion Multiple aneurysms have been described

Statements on its incidence vary Representative figures are 9 per cent (Parkinson et al) 14 per cent (Bean) and even 38 per cent (Libman) of myocardial infarctions In our experience the latter figure more closely approximates the true situation It seems that aneurysm is common in large infarctions

Early aneurysm most often develops with a massive necrosis especially if the blood pressure remains high and the patient is too active

Often the small aneurysmal sac shows a gentle rather than abrupt departure from the normal myocardium There is no sharp bulge In other cases the large sac departs abruptly and may measure as much as 10 cm in diameter Often the aneurysm is partly or completely filled with a thrombus Fortunately pericardial adhesions over the aneurysm are the rule and help to strengthen the thin myocardial wall This may be why rupture of the myocardial sac even in large aneurysms of long standing is relatively rare Most of these aneurysms follow an occlusion of the descending branch of the left coronary artery and are located slightly above the apical region of the left ventricle they occur however in the posterior basal region after an occlusion of the descending branch of the right coronary artery and in other parts such as the interventricular septum

The aneurysm itself causes no symptoms The patient usually has a history of a previous coronary occlusion with infarction although sometimes the occlusion was symptomless Because they were not kept in bed at the time of greatest softening of the myocardial wall that is in the first weeks following the myocardial infarction it is precisely these patients who develop aneurysms

In a large majority the clinical diagnosis of ventricular aneurysms is impossible by all available methods This is true particularly for those aneurysms which do not show a sharp bulge In many cases however the diagnosis is easy

The outstanding sign is an abnormal pulsation usually located slightly above the apex at the left cardiac border or slightly inside it Sometimes this pulsation on the chest wall (a bulging hemisphere) is very strong and can scarcely be suppressed In one of our cases the pulsation was seen in an area 4 or 5 cm in diameter on the sixth day after the symptoms and signs of myocardial infarction appeared Often the pulsation persists throughout the life of the patient but it may diminish in intensity or disappear with the development of thrombi or contraction of scar tissue (Scherf and Erlsbacher)

The location of this pulsation usually distinguishes it from others of cardiac origin It is too high for an apical pulsation too low for one from the pulmonary conus and too lateral for a pulsation of the right ventricle (precordial pulsation)

Dysphagia due to compression of the esophagus by an aneurysm of the left ventricle has been observed (Strandell)

Percussion usually reveals cardiac enlargement The pulse is often small and the systolic blood pressure is often very low

Auscultation often yields indefinite findings such as muffled heart sounds gallop rhythm or even pure and loud sounds Not rarely a systolic murmur is heard and is loudest over the pulsating area in some cases a high pitched diastolic murmur is audible in the same place It has the same character as a murmur of aortic insufficiency (Scherf and Brooks) (figure 78) In two patients observed by one of us the diagnosis of aortic insufficiency was made clinically postmortem examination revealed a cardiac aneurysm It is interesting to note that one of the first cases of cardiac aneurysm diagnosed antemortem presented

a diastolic murmur In this case the murmur had a musical character (Remlinger) In our experience the to and fro murmurs heard over cardiac aneurysms are soft and high pitched The murmurs must be differentiated from extra cardiac murmurs and a pericardial friction rub This is due possibly to the quality of the murmur which makes it similar to those heard in aortic insufficiency During systole the weak aneurysmal sac is filled and distended with



FIG 74 Cardiac aneurysm

blood Backflow of this blood into the left ventricle in diastole may explain the murmur

X ray examination particularly fluoroscopy is of great diagnostic help Frequently the bulge of a large aneurysmal sac reveals the diagnosis immediately Sometimes the sac is visualized only when the patient is slightly rotated Often the abdominal shadow obscures the aneurysm in these cases examination after the administration of sodium bicarbonate has been recommended since this causes a large gas bubble in the stomach with the result that much of the left lower border of the heart becomes visible Apart from the deformed contour of the left cardiac border aneurysms are sometimes recognized on fluoroscopy by abnormal pulsations like marked paradoxical outward pulsation during systole Examination in the right oblique position is often helpful One must

be careful not to confuse the fat pad on the lower cardiac border with a cardiac aneurysm

Figure 74 shows a typical aneurysm at the left border of the heart The electrocardiogram of this patient showed the pattern of an antero lateral wall infarction

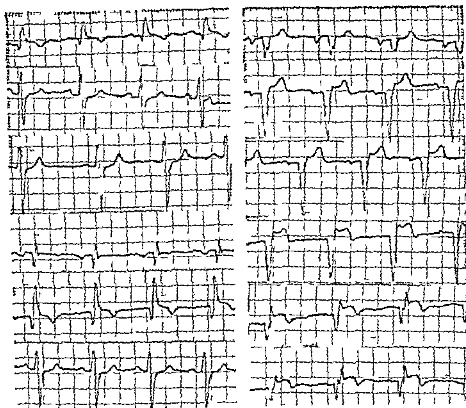


FIG 75 Typical electrocardiogram of an antero lateral wall infarction showing persistent elevation of the RS T segments in lead I aVL V 3 V 4 V 5 and V 6 The aV leads are beneath the standard leads while the chest leads are on the right side

Aneurysm of the basal posterior aspect of the left ventricle may occasionally be visible with a postero anterior chest plate

Often increased rounding of the left ventricle (marked aortic configuration) in a patient who does not have and never had hypertension may point to a cardiac aneurysm (Parkinson et al) If there is a lime salt deposit at an abnormal site along the left cardiac border an aneurysm may be suspected

Even with large aneurysms the diagnosis is often impossible despite careful x ray studies

The electrocardiogram is not characteristic It shows evidence of myocardial involvement and often there are signs of an anterior or rarely of a posterior

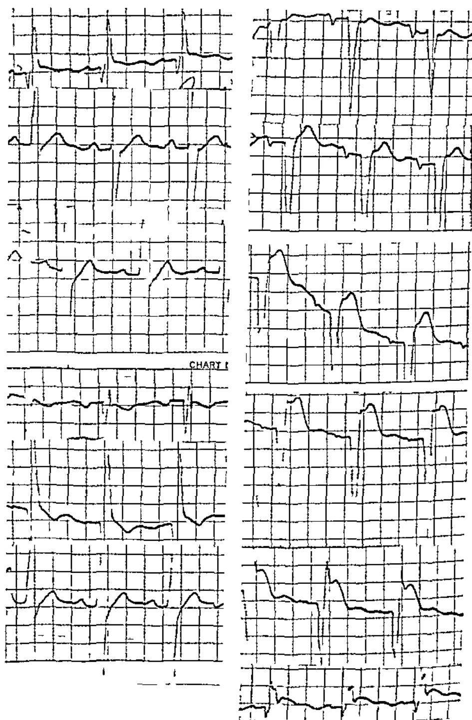


FIG 76 This electrocardiogram is from the same patient as shown in fig 7 but was obtained *27 months later The patient felt well and had resumed medical practice* in spite of his cardiac aneurysm The RS T segments in lead I and the chest leads are still elevated In aVL the T wave remains inverted while the inversion in the chest leads has disappeared The patient died 3 years later

wall infarction In some of our cases a bundle branch block or some of the other changes encountered in coronary disease has been found Many of our patients however showed an unusual persistence of elevation of the RS T segment so that in lead I and in the chest leads one might be inclined to diagnose a recent anterior wall infarction The electrocardiogram shows these features

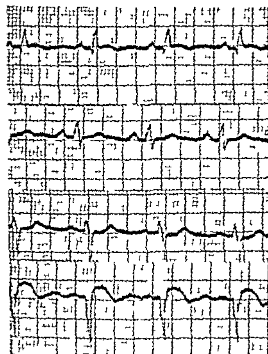


FIG 7 The three standard leads and V 5 of a 70 year old patient with a cardiac aneurysm The clinical diagnosis was confirmed at necropsy Persistent elevation of the I S T segment imitating the pattern of an acute infarction is visible in lead I and V 5 (Courtesy of Dr C Borneman)

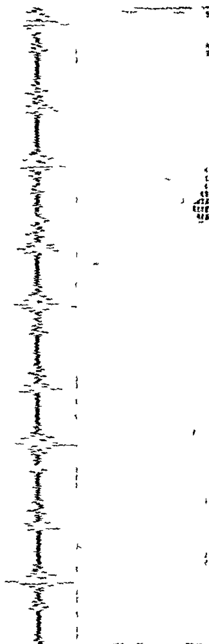


FIG 18 Stethogram of the same patient from whom the electrocardiogram of figure 7 was taken A soft systolic and a louder diastolic murmur are visible (Courtesy of Dr C Borneman)

for many years without further change In our experience if there is a permanent I S T elevation in the electrocardiogram of patients who once had a myocardial infarction the suspicion of a cardiac aneurysm is justified Although this

electrocardiographic pattern is found only in a minority of cardiac aneurysms it is by no means rare

In figures 75 and 76 an electrocardiographic pattern typical for a cardiac aneurysm is reproduced The tracings were obtained from a 56 year old man with a large cardiac aneurysm They show the abnormally deep Q wave with the slight elevation of the RS T segment in lead I and the chest leads

Figure 77 shows the electrocardiogram and figure 78 the stethogram of a patient with a cardiac aneurysm The 70 year old woman showed the typical circumscribed pulsation 16 days after the attack A typical systolic diastolic murmur was heard Postmortem examination revealed an antero lateral wall infarction The wall of the aneurysm was remarkably thin and formed by white translucent fibrous tissue (courtesy Dr C Borneman)

There may be survival of 10 years or more despite a huge cardiac aneurysm One of our patients is active and still free from complaints more than eighteen years after his cardiac aneurysm was recognized Another patient with a cardiac aneurysm which has been present for fourteen years flew over the *Atlantic* 48 times without any discomfort These patients may lead active lives free from symptoms nevertheless it is clear that physical activities must be curtailed

In many reported cases and in 3 personal observations paroxysmal ventricular tachycardias developed shortly before sudden death in patients with cardiac aneurysms so that one may assume death was the result of ventricular fibrillation

In a patient with a large ventricular aneurysm after infarction the aneurysm has been successfully removed by surgery (Likoff and Bailey)

The Shoulder Hand Syndrome and Dupuytren s Contracture These complications are not infrequent following myocardial infarction They were noted in 17 out of 133 consecutive cases of myocardial infarction (Ernstene and Kinell) They occur most often on the left side that is the side to which pain most often radiates Dystrophy of muscles and a tendency to fibrotic changes appear

Not rarely a patient is alarmed by the development of shoulder pain which he takes to be a sign of a recurrence of angina pectoris But because this pain is independent of physical effort and occurs when the arm is moved distinction is easy Early hyperemia and edema of the hand may appear and last as long as six months This hyperemia like that following trauma leads to osteoporosis Abduction and external rotation of the arm are reduced and tenderness is found on pressure on the periarticular tissues of the shoulder The handicapped patient is unable to use the arm freely The syndrome may appear in patients with exertional angina pectoris or even in asymptomatic coronary sclerosis some time before a myocardial infarction occurs It is occasionally seen 3 to 12 weeks after an infarction in other cases months and even years elapse before it appears Naturally the disturbance is not characteristic of coronary occlusion or an acute infarction It is a common occurrence in coronary sclerosis without angina pectoris and without any evidence of infarction

Many attempts have been made to explain these changes Viscero visceral reflexes reflex vascular spasm in the periarticular tissue and resultant nutritional disturbances have been suspected to be determining factors

At the present time it is assumed that afferent stimuli from the heart bombard the internuncial pool which is a network of interconnecting neurons in the central grey matter extending over several segments in the spinal cord From here outgoing stimuli influence autonomic pathways

The disability and pain may last for six months and may recur at any time

It is claimed by some investigators that this syndrome appears particularly in subjects with a certain type of personality that is in those who tolerate pain poorly (Coventry) The process is said to progress faster if the arm is not used

If procaine is injected into the stellate ganglion in the early stages of the syndrome rapid recovery may occur or progression is prevented Cortisone has also proved useful A dose of 75 mg is given daily and with the appearance of improvement the amount is reduced to 50 and then 25 mg Hydrocortisone 50 mg injected into a trigger zone only once is said to help many patients (Berger)

Combined with or independent of these shoulder affections changes may also be noticed in the left (rarely the right) hand The skin is glossy and the hand as well as the fingers become stiff the patient is unable to bend the hand or to make a fist A slight red discoloration appears and the fingers are cold The ulnar side is affected more than the rest of the hand Atrophy of the skin follows These changes were noted in 39 (21 8 per cent) out of 178 consecutive cases of myocardial infarction (Johnson) They may develop as early as three weeks after the infarction Gradually the picture of Dupuytren s contracture develops The lesion may be symmetrical and independent of the site of radiation of the pain

Dupuytren s contracture does not seem to be an entity but may follow any irritation of the sympathetic nervous system It occurs in diverse visceral diseases Here also the possibility of reflex vasoconstriction has been discussed

There is no sharp distinction between these conditions and Sudeck s atrophy and causalgia

Differential Diagnosis

In the preceding sections it has been pointed out that coronary occlusion with myocardial infarction may cause a series of symptoms and signs which readily permit the diagnosis in a vast majority of cases Occasionally however as the result of absence of pain or of abnormal radiation of the pain or due to the fact that pain similar to that observed in coronary occlusion occurs in other diseases the diagnosis is missed In addition certain signs arise due to complications thereby further confusing the clinical picture Moreover now that physicians are more coronary conscious the diagnosis of occlusion with infarction is made at times when the condition is not present

At this juncture it must be re emphasized that the diagnosis should never be made on the basis of the pain alone Even if the pain is typical' lasts for hours is overwhelming in intensity or radiates to the left arm and hand another condition may be present The diagnosis should always be confirmed by one of the signs mentioned previously — elevated temperature fall of blood pressure increased sedimentation rate and so forth On the other hand every complaint of pressure or tension behind the sternum irrespective of how slight it is should arouse the suspicion of the presence of a myocardial infarction when the distress lasts for longer than a few minutes

Epilepsy In patients with many successive attacks of epileptic convulsions or status epilepticus the violent effort caused by tonic and clonic convulsions without adequate breathing causes hypoxia of the heart muscle and myocardial necrosis Neuberger found such necroses in 14 of 34 patients

One must remember on the other hand that patients with myocardial infarction may develop Stokes Adams attacks resembling epileptic convulsions The differential diagnosis must be considered and will usually be possible

Cardiac Neurosis Pain in the cardiac region is common in cardiac neuroses (see neurocirculatory asthenia) In contradistinction to coronary thrombosis the pain is often shortlasting and stabbing although it may be prolonged and severe In this instance it is usually located at the cardiac apex and not behind the sternum The patient indicates the painful area by pointing with the tip of a finger rather than the palm of the hand as in anginal pain of any etiology Occasionally a circumscribed area at the apex will be sensitive to pressure The frequent recurrence of this pain its relation to certain emotional disturbances the absence of organic findings and the presence of the signs of a cardiac neurosis usually permit the diagnosis Occasionally a cardiac neurosis of this type develops after a friend or relative suddenly and unexpectedly died in my arms from a coronary attack

Sensations of an unpleasant character are often noted in the cardiac area by healthy people who may recognize the relation to emotions anxiety and the like While they rarely gain importance and are not associated with heart disease by the average healthy person they may become major problems in anyone who is apprehensive and readily alarmed

It does not seem amiss to stress that very careful examination and observation are necessary before a patient is labeled neurotic The information some patients obtain from pseudoscientific publications in magazines and newspapers occasionally makes it difficult to secure an unbiased history

The Thoracic Cage and Spondylarthritis Osteoarthritis of the upper dorsal vertebra causes distress that is frequently confused with the pain of coronary disease The pain may last for seconds or hours it has the typical radiation to the left or right arm and it may be very distressing Usually there are no objective findings the movements of the upper dorsal vertebrae are sometimes restricted The spinous processes of the first dorsal vertebrae are occasionally sensitive to percussion and a segmental cutaneous hyperesthesia is sometimes

demonstrable X ray demonstration of a hypertrophic spondylitis is diagnostically indecisive since such evidence is secured very often in adults without symptoms On the other hand there may be an extensive hypertrophic osteoarthritis with negative x ray findings

Similar attacks of pain with the same radiation occur in myositis and fibromyositis of the long dorsal muscles in the other thoracic segments

Radiculitis of the upper dorsal spine may cause pain which contrary to some statements may be retrosternal It appears particularly when the patient assumes a certain position in bed and is relieved when the position is altered It also occurs with coughing straining at stool and sneezing At times it appears while the patient is walking and swinging his body here the differential diagnosis from an exertional angina is especially difficult Pressure on the spine or percussion of the spinous processes may reproduce the pain It is noted particularly often in patients with deformities of the spine Certain trigger points release the pain Cases have been observed in which nitroglycerin afforded relief thus making the diagnosis even more difficult

The occurrence of pain that radiates into the left or right arm in these lesions has been clarified by the important work of Lewis and Kellgren by injection of a hypertonic saline solution into the interspinous ligaments and adjacent muscles they produced in the corresponding segments the same type of pain with similar referred phenomena as found in visceral disease If such injections are made into the upper thoracic segments in patients who had a myocardial infarction at some earlier date they produce pain indistinguishable from that of an angina pectoris in myocardial infarction Even the upper chest may feel constricted the retrosternal pain however is missed in such experiments

The differential diagnosis often is very difficult particularly in early stages and problems arise when the pain is so severe that respiration is rendered difficult The situation becomes more apparent after the symptoms have existed for a time and cardiac findings remain negative In this instance as with the cardiac neuroses careful examination and observation over a period are necessary before a positive diagnosis can be made

It is important to note that in some cases of spondylarthritis the pain may be retrosternal and increases or appears on exertion owing to abnormal strain on the somatic structures involved In these cases injection of novocaine into the interspinous ligaments and adjacent structures provides immediate relief X ray radiation of the spine is helpful and most beneficial in chronic cases

In patients with intercostal neuralgia herpes zoster neuralgia of the brachial plexus or a myositis in the corresponding segments the history may be somewhat similar to that of a coronary occlusion but a careful examination usually permits differentiation In the first hours before the herpetic eruption appears however the diagnosis may be difficult since negative cardiac findings can be encountered in cases of coronary occlusion An important and common

type of pain in women with endocrine disturbances will be discussed in the appropriate section

Pulmonary Embolism As pointed out before this event occasionally provokes a syndrome very similar to that of myocardial infarction In both conditions there may be the same prolonged pain the same radiation and localization Fall of blood pressure leukocytosis fever increased sedimentation rate hemoptysis pericarditis and even similar electrocardiographic alterations are observed in some patients The differential diagnosis may be difficult or impossible The task of distinction is rendered harder by the fact that many patients with myocardial infarction develop a peripheral venous thrombosis owing to the enforced rest in bed and the disturbance of circulation The so called second attack which develops a few days or weeks after coronary occlusion is due in many cases to a pulmonary embolus although the symptoms may be almost identical to those experienced during the development of the myocardial infarction In all attacks of this type that appear in bedridden patients pulmonary embolism should be suspected The differentiation is easier if the electrocardiogram shows the typical pattern of myocardial infarction or pulmonary embolism respectively In both conditions however occasionally only indefinite changes appear The absence of an increase of transaminase in the blood speaks for pulmonary embolism But positive tests in pulmonary infarction have been reported

Pneumonia If the patient does not have much anginal pain but dyspnea fever and rales over circumscribed areas of the lungs are present the diagnosis of pneumonia is sometimes made Formerly this happened frequently but now the mistake is unusual In a similar way a left sided pleuritis was often diagnosed and the provocative infarction overlooked

Spontaneous Pneumothorax This and spontaneous mediastinal emphysema may cause prolonged severe retrosternal pain with radiation toward the shoulders but the differential diagnosis is easy

Gastrointestinal Disease Many disturbances of the gastrointestinal tract may simulate coronary occlusion Esophageal spasm may cause excruciating pains often situated behind the lower sternum It may spread to the jaw or into the arms lasting for hours Some patients report benefit from nitroglycerin In others only a dull ache is experienced Retrosternal pain occurring at night and often sufficiently severe to require demerol or morphine for relief is sometimes noted in carcinoma of the esophagus Since dysphagia may be minimal or absent in these cases and the attack does not occur in connection with eating prolonged episodes may lead to the erroneous diagnosis of actual or impending coronary occlusion

It is very common to note severe pain radiating to or perceived only in the left chest or shoulder in colonic spasm Distention of the splenic colon can cause precordial pain and pain spreading into the left arm The pain noted in connection with these colonic disturbances may be severe and prolonged Peptic ulcer cholelithiasis and cholecystitis occasionally present pain that is located exclusively

in the chest if this pain happens to be felt only on the left side the diagnosis of a possible coronary disease may arise

Gallbladder Disease The incidence of gallbladder attacks is greater in patients with coronary sclerosis than in the general population The fact that gallbladder disease and myocardial infarction may coexist creates a difficult diagnostic problem in some patients An attack may begin as a typical gallstone colic and in the convalescence or following surgery myocardial infarction may follow

In gallstone colic the pain may be substernal and may radiate into both arms

Damage to the heart from gallbladder disease has frequently been mentioned The disappearance of arrhythmias following removal of the gallbladder has been reported but such statements must be accepted with considerable reservation

Jaundice temperature leukocytosis and tenderness in the region of the gallbladder (liver) follow a gallstone attack as well as myocardial infarction

Of greater importance on the other hand is the fact that a variety of gastrointestinal symptoms appears in patients with myocardial infarction If the anginal pain happens to be slight or absent mistakes are possible

It is common knowledge that a cardiac infarction may simulate an acute abdominal condition This was clearly demonstrated in early clinical observations on this condition when the occurrence of a status gastralgicus was emphasized The pain in coronary occlusion may be exclusively abdominal If it is so intolerable that the patient is unable to move — if the abdominal muscles are rigid and there is associated shock and vomiting — the diagnosis of a perforated peptic ulcer or pancreatic necrosis is comprehensible Physical examination of the heart may disclose nothing abnormal despite a large myocardial infarction other methods of investigation such as the electrocardiogram or x ray (to detect a bubble of gas beneath the diaphragm) may not be available and such patients have undergone surgery

Sometimes laparotomy appears necessary but physicians refuse to operate because the patient reported some cardiac symptoms of long duration and because positive cardiac findings were present accordingly the diagnosis of coronary occlusion with abdominal symptoms seems logical At necropsy peritonitis associated with a perforated peptic ulcer was found We have seen single cases of a combined coronary occlusion and perforated ulcer and one of coronary occlusion and acute hemorrhagic pancreatitis

As an aid to differential diagnosis it may sometimes be helpful to remember that cardiac infarction with abdominal pain does not cause the boardlike rigidity of the patient with a perforated viscus on the other hand a closed perforation may also fail to present this rigidity

If pain is experienced only in the right upper abdominal quadrant cholelithiasis may be suspected if fever leukocytosis hepatic enlargement and jaundice develop cholecystitis is often diagnosed

Confusion with acute gastritis or gastroenteritis is less common than even fifteen years ago If pain was absent or slight and localized in the epigastrium—

while nausea vomiting and diarrhea (due to visceral reflexes) were in the fore ground *acute indigestion was a common diagnosis Sudden death due to* overeating or to acute dilatation of the stomach so often described in older literature was usually due to coronary occlusion

Esophageal Hiatus Hernia This abnormality causes a syndrome that is easily confused with coronary disease and coronary occlusion Three forms of this disturbance which is most common in obese women who are stocky in build and who have had several children are known First the congenitally short esophagus formerly considered common and now regarded as rare if indeed existing at all Second para esophageal hernia which is a true hernia Here the anterior part of the fundus rolls into the chest in front of and lateral to the esophagus (rolling hernia) The sphincter action of the esophagus is intact Third the sliding hernia or esophago gastric hernia, which represents the most common type In this instance perhaps owing to a defect of the diaphragm reflux of food and acid from the stomach occurs Esophagitis appears with easy bleeding from the inflamed mucosa Shrinking of the connective tissue and scar formation make the esophagus appear shorter and part of the cardiac portion of the stomach appears in the chest

Nuzum found a hiatus hernia in 12 27 per cent of 957 persons examined He found it in 25 per cent of patients with true angina pectoris Thus the two conditions may and often do coexist

There are all variations between no complaints at all and excruciating crippling pain not rarely retrosternally and spreading to the jaw or both arms Pains occur at night

Symptoms may appear at any age but most patients are beyond 40 years Fullness during or shortly after meals regurgitation belching hiccough nausea and vomiting are common All these complaints however are also found in coronary disease and myocardial infarctions

About one third of the patients complain of substernal pain This pain may radiate into the left shoulder and even into the left arm Belching may give immediate relief Considerable anxiety and distress may be present Sometimes the pain appears on exertion and is relieved by nitrites (Jones) According to Donnelly contraction of the abdominal muscles on walking increases intra esophageal pressure and this leads to pain in patients with esophagitis Pain on stooping is common for similar reasons The patient may feel particularly uncomfortable at night and often experiences the nocturnal distress while lying in bed immediate relief is secured by standing This point in the history is rather characteristic

The diagnosis is often confirmed by x ray examination which should be made in the Trendelenburg position Often however the hernia does not appear on tilting but is demonstrated when the patient bends forward Roentgen examination may be temporarily negative

Electrocardiographic changes appear (Cossio and Fustinoni Kaiser) which like the pain have been explained by reflex changes in the coronary blood flow

or have been initiated by mechanical irritation of the vagal fibers in the esophageal hiatus However since the lower esophagus derives its sensory innervation from the fourth to sixth thoracic segments the pain may be truly referred The rapid response to nitroglycerin and the changes in the electrocardiogram seem to favor the first explanation

Treatment is surgical in some cases The administration of alkalies and the use of frequent small feedings of a bland nature are usually recommended and sometimes help Phrenic crush may give relief

Peptic ulcer frequently develops at the level of the esophageal hiatus if it bleeds the patient may suffer from severe anemia

Internal Hemorrhage Patients with an acute and profuse hemorrhage from a peptic ulcer or cirrhosis of the liver may present a syndrome of prolonged sudden severe anginal pain with radiation to the left arm shock and collapse In 16 out of 18 such cases very distinct changes were demonstrable in the electrocardiogram (Scherf et al) therefore the differentiation from coronary diseases may be difficult Mistakes are particularly liable to occur when there is no hematemesis and when the appearance of tarry stools is delayed for two or three days A marked anemia also need not be present since the acuity of blood loss rather than its quantity causes the symptoms and the electrocardiographic changes

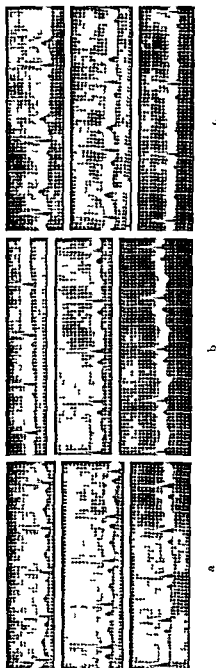


Fig 49 A series of tracings from a patient with an acute profuse internal hemorrhage (the three standard leads are beneath each other)

General vasoconstriction occurs following blood loss and involves the arteries as well as the veins there is an adjustment of the vascular bed to the diminished amount of blood (Bazett) This seems to be effected by carotid sinus reflexes when the arterial blood pressure shows a tendency to fall and by reflexes from the veins There is

a general vasoconstriction following a fall in venous pressure (McDowall reflex)

For a long time it was believed that this homeostasis was necessary to protect vital organs like the heart from a reduced blood supply The frequent finding of electrocardiographic changes after an acute blood loss shows however that the coronary arteries participate in the general vasoconstriction The anginal pain disappears in a few hours and the changes in the electrocardiogram vanish in a few days even if there is no improvement in the status of the red blood cell count

In figure 79 electrocardiograms in the three limb leads are reproduced These were taken from a 32 year old male who was admitted for an acute hematemesis from a duodenal ulcer Figure 79a shows the electrocardiogram obtained immediately after admission i e about six hours after hemorrhage It shows only a sinus tachycardia The second electrocardiogram registered about 20 hours after the hemorrhage shows abnormal T waves in each lead The third tracing was obtained five days after the first one and is normal

It seems that the changes appear not earlier than 6 or 7 hours before and not later than 18 to 20 hours after the hemorrhage They disappear in a week to 10 days

If the myocardium of an animal is examined following an acute blood loss necrosis in the subendocardial layers is found which is typical of a diminished blood (oxygen) supply to the heart

The occurrence of coronary thrombosis in patients with coronary sclerosis has been observed following an acute internal hemorrhage

Blindness following hematemesis or other forms of hemorrhage may also be explained by the reflex vasoconstriction (Black Levatin)

Acute Pericarditis It was noted earlier that this lesion is sometimes associated with severe precordial pain which lasts for hours Since the epicardium and a great part of the parietal pericardium are insensitive to painful stimuli some have assumed that irritation of the sensory fibers at the base of the heart where the epicardium reflects into the pericardium accounts for the pain Mediastinitis is a more probable cause If this pain is present in a patient with pericarditis it may be difficult to decide whether a tuberculous rheumatic or pneumococcic pericarditis is present or a pericarditis following myocardial infarction The electrocardiogram often but not invariably offers assistance in the differentiation

Other Causes Frequently severe pain occurs in an attack of paroxysmal tachycardia during a hypertensive crisis and in women with disturbances of ovarian function as will be discussed later These conditions may also be confused with the pain of myocardial infarction

The difficulty of differentiation between myocardial infarction and dissection of the aorta will be discussed later in the book

Prodromal Symptoms

In a large percentage of patients there are no symptoms before the appearance of coronary occlusion and myocardial infarction The first attack strikes like lightning

Some patients have had an angina on effort for years These patients may develop the prolonged pain due to myocardial infarction suddenly and without premonitory signs In others however the imminent threat of coronary occlusion can be predicted in this group attacks begin to appear at rest they last longer are more severe and nitroglycerin affords progressively less relief Under these circumstances it is wise to keep the patient quiet and to take the necessary steps for the imminent emergency (administration of vasodilators) Patients with prodromal symptoms are not rare The classic picture of myocardial infarction need not develop however because a slow and painless fibrotic occlusion may develop or collateral circulation may become active and prevent an infarction even in the presence of a coronary occlusion

Some patients who develop a myocardial infarction describe some minor attacks they had — a few days prior to the major episode — that lasted for only a few minutes these attacks were so slight they were disregarded

Prognosis

If a coronary thrombosis has occurred sudden death may follow at any given subsequent moment Sudden death is also common in coronary sclerosis and coronary involvement secondary to aortitis In a series of 198 instances of sudden death coronary disease was demonstrable in 104 at necropsy valvular diseases and various kinds of aneurysms were next in order (Bedford)

Formerly the immediate mortality of the first attack was regarded as much higher (53 3 per cent) (Levine and Brown) than at present (10 to 15 per cent) Some authors report an immediate mortality of only 10 per cent which would agree with our experience in patients who survive the first few hours Statistics of this kind necessarily depend upon the material patients who die suddenly before a physician is called or even before uttering a complaint are not included in statistics Statistics also depend upon a definition of the word immediate Among U S soldiers under 40 years of age Yater et al found an immediate death in 16 per cent death in 15 minutes in 10 per cent An additional 5 per cent of the patients died within 2 hours Among the patients who reached the hospital 18 per cent died within 24 hours and 12 5 per cent later

The causes of death are ventricular fibrillation shock cerebral emboli congestive heart failure and cardiac rupture The first three weeks are particularly precarious

The prognosis is worse as pointed out earlier if extrasystoles or paroxysmal tachycardia appear if the systolic blood pressure falls below 80 mm Hg if there is severe dyspnea and pulmonary congestion or early shock The mortality in the first attack seems to be greater if the patients were previously hypertensive

and the prognosis in the second or third attack of myocardial infarction is worse than in the first one

On the other hand a patient often recovers to such an extent that he leads a normal life for years without complaints The average duration of life in a series of 101 cases (Rosenbaum and Levine) was 41 months One fourth of these patients died within a year one half within two years and three fourths within five years The status of the other coronary arteries is decisive for the outcome We believe that the figures would be more encouraging if all infarctions occurring in practice were included

In one observation a patient had his first attack of coronary thrombosis when 40 years old and the second when 75 years old A third attack occurred in his seventy eighth year The patient died at 80 nearly 40 years after the first attack (Drake)

Instances of myocardial infarction in pregnancy with successful delivery are known (Antonius et al) However many patients succumb

Sooner or later a large number of patients develop left ventricular failure and pulmonary engorgement A large percentage of patients who do not have exertional anginal pain prior to the attack have pain even in bed after the episode and are particularly apt to complain of anginal pain on effort

It seems advisable to stress once again that patients with coronary disease even if their condition seems satisfactory may present very serious complications or may succumb suddenly at any moment but there are cases on the other hand in which the patients were unconscious with unbelievably low blood pressures and almost inaudible heart sounds who recovered and lived normally for many years

Accordingly the prognosis should never be regarded as good even when the patient has a very light attack and seems well off on the other hand it should never be absolutely hopeless There are few cardiac conditions in which the unexpected happens more often Surprises are encountered in both directions

TREATMENT

General Measures Not only physical but also mental rest is important The patient is put at ease and is reassured he is told that he had a vascular spasm in the heart (the word thrombosis is avoided) From the beginning he is examined and controlled constantly as if he were in a diabetic coma A simple light case might become an emergency at any moment Later he is examined at least twice and then once daily Even the excitement of ward rounds may cause a fatal accident (Jarvinen)

Pain The severe anginal pain accompanying an acute coronary thrombosis requires demerol or morphine (or pantopon) The initial dose of morphine should be 0 015–0 02 Gm and it is well to add some atropine (0 5 mg) to the first injection of morphine sulfate In many cases it will be necessary to follow the first injection after 30 minutes with a second or even third occasionally even

this fails to relieve pain We have seen patients toss restlessly and complain bitterly about excruciating pain after having received more than 0 06 Gm of morphine within three hours Demerol causes less side effects and less respiratory depression and is preferred In these cases phenobarbital affords little relief infiltration of the skin in the area to which the pain is referred has been recommended but provides no relief in our experience Paravertebral anesthesia helps immediately but is rarely done because one always hopes that the pain will disappear in the next hour The distress may persist however with unabated intensity for 24 hours or more and may exhaust the patient completely

Oxygen Persistent pain threatening shock arrhythmias and even marked fall of blood pressure are indications for the administration of oxygen With a nasal catheter and a flow of 5 to 6 liters per minute the concentration reached is only 30 per cent With a tent and a flow of 12 to 13 liters the concentration is 40 to 50 per cent It reaches 70 per cent with a mask and is given for 5 to 6 hours and then removed for short intervals The patient who is frightened by the suggestion of oxygen is reassured and told that it takes the load off the heart It is wise not to wait until complications develop but to administer oxygen for the first few days in every patient when the evidence speaks for the presence of a larger infarction

Anticoagulants The use dosage indications and contraindications of anticoagulants have been discussed in a preceding chapter At this point it is appropriate to discuss their use in patients with myocardial infarctions

In myocardial infarction danger arises from both intracardiac thrombi which may cause systemic embolism and thrombi formed in the peripheral veins which produce pulmonary embolism during the period of rest Because of the high incidence of these complications and the discovery of hypercoagulability of the blood after an infarction the Committee of the American Heart Association under the Chairmanship of I S Wright has recommended treatment with anticoagulants in all cases of coronary thrombosis with infarction unless such therapy is contraindicated This recommendation is based upon the experience gained from over 1000 observations It was found that thromboembolic phenomena appeared in 41 8 per cent of the control (untreated) subjects while they appeared in only 13 1 per cent of the treated cases Among the controls 23 4 per cent died within 6 weeks while in the treated group only 16 per cent died These differences are statistically significant even if one considers that an occasional patient may die from consequences of therapy and that the percentage of cardiac rupture and pericardial hemorrhage is 2 per cent of untreated cases and 4 per cent of treated ones The value of anticoagulants was particularly evident in obese patients and those with congestive heart failure

Lately it has been recommended that only the severely ill (poor risk) patient be treated with anticoagulants and that these compounds be omitted in the mild (satisfactory) cases This seems to be the current attitude of most cardiologists in this country In our opinion however this attitude is not justified As stated earlier a clinically mild case may suddenly turn into a severe one

the appearance of thromboembolism in mild cases can never be predicted. Actually, those who have seen a mild case recovering nicely suddenly develop cerebral embolism resulting in a permanent hemiplegia or a peripheral embolism necessitating amputation of one leg, will be hesitant to treat only severely sick patients with anticoagulants. Good risk patients exist only in retrospect (Gilchrist and Tulloch). One must always keep in mind that the administration of anticoagulants does not abolish but merely reduces the danger of thromboembolism, while at the same time adding new dangers, the possibility of hemorrhage and cardiac rupture with hemopericardium.

It has been claimed that in patients with myocardial infarction treated with anticoagulants, cardiac failure is less common and recovery from shock occurs more readily.

One of the disadvantages of therapy with Dicumarol or similar compounds is that, according to the investigations of Wright's Committee, no satisfactory preventive effect is accomplished unless the prothrombin time is kept at levels between 25 and 30 seconds. This is difficult to establish; prothrombin times of over 30 often lead to bleeding. We try to keep the patient's prothrombin time at double the control value.

The treatment is not applicable to patients with blood dyscrasias, bleeding ulcers, hypoprothrombinemia (vitamin K deficiencies, liver damage), renal damage and insufficiency, anemias of various etiologies, late pregnancy, open wounds, subacute bacterial endocarditis, and postoperative drainage of viscera.

Most physicians do not give heparin at the beginning. Therefore, the patient often remains unprotected for the first few days in which most thrombi form. The administration of heparin should start immediately after the diagnosis is made if the patient is to be protected as far as possible. If future investigations show that injection of concentrated heparin (1 ml. containing 100 mg.) every 12 hours protects the patient from thrombus formation even during the period when the coagulation time returns to normal before the next injection is due, a relatively safe method will be available. We prefer this procedure at the present time.

It is often stated that anticoagulant therapy should be given for 21 to 30 days. In our opinion such treatment should be continued until the patient is fully ambulatory. In order that rebound phenomena be prevented, the dose is gradually diminished over a few days instead of therapy's being discontinued abruptly.

Nichols used anticoagulants as a prophylactic measure over a period of years in patients who had recovered from one attack, and it was recommended in patients with the premonitory syndrome when an attack threatened. Our experience concurs with that of others — we believe that this therapy should not be used. Since rupture of giant capillaries in the atherosclerotic area of the coronary artery is a frequent cause of coronary thrombosis, this treatment may be harmful; in four patients with the premonitory syndrome we observed coronary occlusion following soon after such therapy. Nichols himself is very

cautious in his conclusions In some publications in which this treatment is recommended as a good prophylaxis the published electrocardiograms show that the patients had infarctions during the therapy that had not been recognized by the authors It has been found however that the mortality rate of those patients in whom preventive long term anticoagulant therapy was used is lower (Suzmann et al)

Of all investigators pleading against therapy with anticoagulants no one is more articulate than Evans Let it go now before remorse weighs too heavily on those who may continue for a little longer to advocate its use

Shock When shock is impending the patient should be hospitalized He should be placed in the horizontal position and administered oxygen One should examine the patient carefully for evidence of cardiac failure (pulmonary congestion engorged neck veins) which may be present simultaneously and which needs special therapy Demerol should be administered It is evident that in the presence of or with impending pulmonary edema the intravenous administration of blood or plasma may be injurious

Success has been reported from the intravenous or intraarterial infusion of blood plasma or plasma substitutes When shock occurs because of a diminished cardiac output that results from direct cardiac damage success should not be expected indeed often harm will be done It is recommended that more than 300 ml of plasma or blood not be administered despite the fact that some authors advocate as much as 1000 ml The rate of infusion also varies some recommend not more than 2 ml per minute while others permit 100 ml per minute For the intraarterial infusion the exposed radial artery is used

The best plasma substitute is dextran recommended by Swedish workers It is a polysaccharide obtained through enzymatic action with a molecular size similar to that of plasma proteins Dextran has little pyrogenic or antigenic action and is very slowly excreted without being metabolized therefore it circulates in the body for days

Pressor amines have been used for years especially neosynephrine which has the advantage of creating fewer arrhythmias than epinephrine It is given hypodermically or intramuscularly (10—15 mg) and is repeated as often as necessary that is whenever the blood pressure falls In recent years the effect of norepinephrine has been widely studied Most authors advise its use since in small doses it has predominate effect on the peripheral vessels while the cardiac effect is minimal Norepinephrine also raises cardiac oxygen consumption much less than epinephrine and it causes fewer dangerous ventricular arrhythmias than epinephrine although this action is not completely absent as some claim In some animals norepinephrine widens the coronary arteries its action in man is unknown The disadvantage of the substance is that it must be given in an infusion one ampule (4 mg) is diluted with 500 cc of saline or 5 per cent glucose First administration is 10 drops per minute the dose is then regulated according to the blood pressure and the appearance of arrhythmias In recent years isopropylar enol (Isuprel) has been used (10 mg) For quick action

linguets are available Wyamine (mephenteramine) is given in doses of 15—30 mg intramuscularly as often as necessary

In one patient 402 mg of Levophed were given during a period of 14 days The patient recovered (Siglin)

Dehydration This condition with all its attendant dangers is common and results from the vomiting and profuse perspiration The physician in charge must avoid the administration of large amounts of fluid because of the danger of pulmonary edema Hypodermoclysis is often necessary

Vasodilators It is useful to administer vasodilators early because the fate of patients depends to a great extent on the function of the collateral circulation We prefer slowly released nitroglycerin e g Nitroglyn (gr 1/10) The experiments of Zoll and Normann demonstrated the significant effects of nitrites in the creation of functioning interarterial coronary anastomoses Papaverine hydrochloride and aminophylline are also recommended Neither drug should however be given intravenously to patients with acute coronary thrombosis In therapeutic doses papaverine is harmless for a healthy and even a slightly damaged myocardium but the effects are quite different if large doses are given intravenously to a patient with a damaged heart Experimental studies on the cardiac action of papaverine in patients with damaged hearts are scarce Our clinical experience with intravenous injections of papaverine in patients with a fresh coronary occlusion is not satisfactory but there is no objection to an intramuscular injection of 0 04 to 0 06 Gm Likewise aminophylline should not be given intravenously to patients whose blood pressure shows a tendency to fall Since intramuscular injections are usually painful a rectal suppository of 0 5 Gm of aminophylline should be inserted twice daily

While we consider aminophylline to be one of the most effective vasodilators available it should be pointed out at this juncture that on the basis of experimental studies purine bodies (caffeine theobromine) particularly theophylline increase the coagulability of the blood The coagulation time may be shortened by 50 per cent Lately it has been found that these substances in a dosage equivalent to that given in man cause hyperthrombinemia Since clinical investigations confirm these results serious objections must arise against the use of theobromine caffeine and theophylline in patients in whom the danger of thrombus formation exists For a time our results were not confirmed Recently in Seegers laboratory it was found that Ac globulin which tremendously enhances *the conversion of prothrombin into thrombin is increased in the dog* by more than 100 per cent by aminophylline The dose however is large — 0 1 Gm. per Kg Seegers also reports that larger doses of Dicumarol are necessary if aminophylline is given simultaneously (McCormick and Young) In a few cases of coronary sclerosis with angina pectoris we observed coronary thrombosis following intravenous injections of aminophylline

Quinidine Another emergency measure is the administration of quinidine We give 0 2 Gm every four hours routinely to all patients with a fresh coronary occlusion to prevent dangerous extrasystolic disturbances of rhythm If extra

systoles occur in spite of this regimen the dose may have to be increased (figure 80) If a paroxysmal ventricular tachycardia complicates coronary thrombosis doses up to 2 0 Gm of quinidine sulfate daily may be necessary The danger of a tachycardia in a case of recent myocardial infarction is greater than the possible harm which might be caused by larger doses of quinidine

The present custom not to treat prophylactically with quinidine but to use the drug only immediately when extrasystoles appear is strange It is based

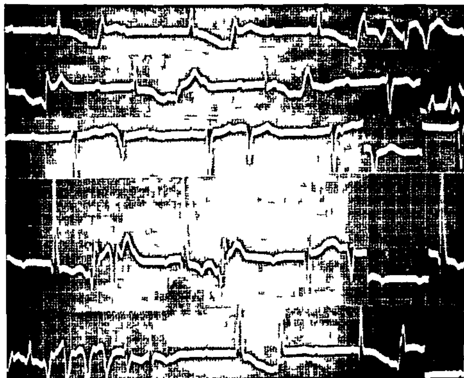


FIG 80 In a 59 year old man with a myocardial infarction complete heart block appeared with massive inversion of the T waves Multiple multiform ventricular extrasystoles appeared These are the extrasystoles which often precede ventricular fibrillation Occasionally abnormal ectopic idioventricular beats are also visible

mostly on experiments on animals which are not comparable to clinical cases of coronary thrombosis for two reasons One is the fact that dogs (on which many experiments were done) develop ventricular fibrillation in 30 per cent of the cases after ligation of the coronary arteries When quinidine therapy that is started prior to ligation in such animals fails to diminish the incidence of fibrillation it may be because of overwhelming impulses Man may respond differently Actually extrasystoles that appear following coronary occlusion disappear in man quickly if quinidine is given in most instances

A second reason for the lack of correlation between animal experiments and clinical cases of coronary thrombosis is that in most experiments quinidine was given intravenously in such doses that apnea and diastolic cardiac standstill occurred This explains why in some statistics the mortality in animals who received quinidine before ligation of the coronary arteries was even higher than in the controls

In a clinical investigation Boone and Pappas found a mortality of 16 per cent in patients with myocardial infarction who received 0 2 Gm of quinidine every 3 hours while awake The mortality in 127 untreated subjects was 35 per cent

Other Measures Nitroglycerin is given if temporary attacks of anginal pain recur

For patients with heart block temporary cardiac standstill and attacks of Stokes Adams syndrome the administration of aminophylline in the form of suppositories usually suffices Occasionally 30 mg of ephedrine must also be given three times a day in this group of cases to prevent new attacks of Stokes Adams syndrome Linguets of isoprel are also useful

Bed Rest Often absolute rest cannot be enforced during the acute pain for the patient may feel compelled to move by anxiety and restlessness When the pain eases and patients have less pain from the start strict bed rest is ordered The patient is told to lie quietly on his back and to avoid turning from side to side the main objective is to relieve every possible strain on the heart since movement may increase cardiac activity Even during the period of strict bed rest the patient is advised to wriggle the toes (venous thrombosis often begins in the sole of the foot) and to bend the knees slowly from time to time and keep them bent for a while if the condition forbids active moments an attendant should perform passive exercises by bending the lower extremities at the hip and knee joints This should be repeated often during the day and should begin immediately after bed rest is enforced in order to lessen the incidence of thrombosis in the lower extremities and the pelvic veins Slight elevation of the lower end of the bed is useful and the application of an elastic bandage on the lower legs is indicated in order to speed up blood flow in the deeper veins

All these measures warrant careful consideration if the common and serious complication pulmonary embolism is to be averted

Recently chair treatment was recommended by Levine In this therapy the patient is permitted to sit in a chair within the first few days after an attack While the procedure need not be harmful in cases of little infarctions it is certainly dangerous with large ones It must be pointed out that among 115 consecutive necropsies performed on patients in a mental institution 16 of 22 cases with myocardial infarction died of cardiac rupture (Jetter and White) This is the type of patient who does not rest in bed after an infarction

The risk of thrombosis of the veins of the leg and pulmonary embolism is increased when patients sit quietly in the chair for hours This danger threatens even if anticoagulants are given

In other investigations it was recommended that a commode be used instead of a bedpan The oxygen consumption with the use of a commode was found to be less than with a bedpan from this it was concluded that with the former less energy is expended Patients who used the bedpan however were advised to perform the Valsalva experiment (i e to force) a procedure which no patient with an acute or old infarction should ever be permitted to do this effort increases the oxygen consumption

In patients with prostatic hypertrophy bed rest may lead to urinary retention which should be taken care of

Mental rest must also be enforced Telephone calls visitors and other disturbing influences should not be permitted

The period of absolute bed rest should last at least three weeks for patients with a marked fall of blood pressure distant heart sounds, pulmonary congestion gallop rhythm or tachycardia If clinical findings are satisfactory strict rest is enforced for only 10 days After this period permission is granted for the patient to turn slowly on one side or the other Not until five weeks pass however do we allow the patient to sit up in bed and in severe cases the period of continuous recumbent position is prolonged until the clinical findings are satisfactory Sometimes low blood pressure muffled almost inaudible heart sounds tachycardia and the tendency to congestive heart failure compel one to insist on a much longer period of bed rest We have repeatedly seen patients whose condition during a period of six to eight months did not justify granting permission to leave the bed In one of our patients bed rest for 11 months was necessary before improvement was regarded as sufficient This patient has been active despite the development of a cardiac aneurysm and has been free from symptoms for ten and one half years

If however in patients who suffered even from severe pain the fall of blood pressure later is only moderate the heart sounds remain loud and the sedimentation rate is only moderately accelerated the bed rest may be shortened to about three weeks This is common in anterior wall infarction or infarctions without changes of the QRS complex in the electrocardiogram In little infarctions to be discussed below bed rest of 7 to 10 days suffices and bathroom privileges are permitted from the beginning of convalescence

It should be stressed once more that the clinical impression is more important than the laboratory findings in making the decision with regard to the maintenance of bed rest While connective tissue appears in the necrotic area in a few days firm healing requires at least eight weeks (Karsner and Dwyer Mallory et al) The electrocardiogram may show progressive improvement even four to eight months after the attack

In a large infarction when the time for bed rest is over the patient is permitted to sit up in bed at first only for a few minutes but gradually for longer periods after a week he is allowed to dangle the legs About two weeks from the day he first sat up in bed the patient may sit in an easy chair near his bed Another week elapses before the patient may walk freely about his apartment

or room With the gradual restoration to normal activities under continuous observation highly satisfactory results are obtained

Permission for the patient to resume his usual occupation subsequently depends upon the progress of his recovery and on the occupation Obviously a patient with a sedentary occupation may return to work earlier than one who does manual labor the latter must usually seek a new type of work

Since the pain disappears within a few hours or days after the onset of the attack and the succeeding soreness is equally transient it is often difficult to convince patients that rest in bed is necessary In this instance it is advisable *to explain that a wound in the heart must heal just as a fractured leg* and this takes time Phenobarbital and the new tranquilizers will prevent patients from becoming too restless

Food At the same time the intake of food is restricted The vomiting that occurs on the first day often makes it impossible for the patient to take any food Later tea fruit juices consommé and milk are given Solid food may be added on the third or fourth day if the patient s condition permits it However the patient must be warned against heavy meals even in the future Frequent small feedings represent the method of choice About 1500 to 1800 calories usually suffice for the bedridden patient and care must be taken to have the food easily digestible and appealing to the patient

Bowel Movements It is safe to allow three days to pass without the patient having a bowel movement On the evening of the third day, a mild *cathartic* — milk of magnesia cascara sagrada or mineral oil — may be given if necessary For patients in a serious condition this is much better than an enema Straining and forcing at stool should never be permitted The patient is advised never again to strain in order to evacuate the bowels Against meteorism a rectal tube is inserted and heat is applied to the abdomen

Sexual Intercourse Smoking The former is forbidden for a variable time but at least for four months The exact period will depend upon the condition of the patient Smoking is forbidden but moderate amounts of alcohol are allowed

Insulin In diabetics with coronary sclerosis and anginal pain particularly in those with a recent myocardial infarction the use of insulin should be avoided as long as possible Even a blood sugar of 200 mg per cent need not *constitute* an indication for the administration of insulin Acidosis uncontrolled by diet or preparation of a patient for operation may necessitate its use

While large doses of insulin often do not influence the heart directly and diabetics with coronary sclerosis take insulin without harm for years there are indisputable observations which indicate that even small doses of insulin may aggravate the cardiovascular situation in some individuals and may even occasion anginal attacks This may be explained by the increased secretion of adrenalin causing tachycardia and hypermotility of the heart when the blood sugar falls If insulin is necessary hypoglycemia should be carefully avoided and vasodilators should be administered at the same time

Digitalis A very important and frequently disputed question involves the permissibility of prescribing digitalis to patients recovering from a recent attack of coronary thrombosis It has been argued that digitalis is harmful because it narrows the coronary arteries furthermore it increases the vigor of contractions thus bringing the danger of cardiac rupture or of embolism from mural thrombi In the first acute phase of myocardial infarction rales at the bases of the lungs or a moderate enlargement of the liver are very frequent This alone is not sufficient to indicate digitalis therapy Even if the rales increase and dyspnea with cough appears it is possible in a vast majority of cases to provide subjective relief to prevent the appearance of pulmonary edema and to diminish the rales by small doses of morphine or pantopon (0 01—0 015 Gm) Within a short time as late as eight or ten days the rales usually disappear under the treatment outlined above without resort to digitalis

When cardiac failure progresses despite rest and the administration of morphine digitalis must be given since no other therapy corrects the situation This will be necessary more often when the blood pressure has been high before the occlusion and does not fall appreciably in the attack In patients with a hypertrophic and dilated left ventricle digitalis gives better results than in congestive failure of a patient with a left ventricle which is normal save for a circumscribed necrosis due to myocardial infarction

Not rarely patients who had a myocardial infarction and begin to walk around or start working develop congestive heart failure or attacks of pulmonary edema They respond readily to digitalis which is required for several months Gradually with the consolidation of the myocardial scar the doses of digitalis can be diminished and one day omitted Rarely more than 0 2 gram of digitalis leaves daily are needed

Surgery Elective surgery will be postponed until four months after the attack In general surgery is tolerated well in coronary heart disease with judicious and cautious use of anesthesia (Keys et al)

Air Travel We permit patients who have had a myocardial infarction of average severity and who have fully recovered to fly four months after the attack It is clear that no patient who has congestive heart failure tachycardia or hypotension should be permitted to fly

At levels over 7 000 feet patients with coronary sclerosis should be given oxygen This is the level at which most pressurized airplanes fly

CORONARY STENOSIS AND ANGINA ON EFFORT

Atherosclerotic stenosis of the branches of the coronary arteries or stenosis of the orifices secondary to syphilitic aortitis are responsible for the classical angina on effort so admirably described by Heberden

If an angina on effort begins suddenly the occurrence of an asymptomatic occlusion of a coronary artery should be considered At post mortem in patients with angina on effort at least 1 and often 2 coronary arteries will be found occluded

INCIDENCE

In this condition the history is of paramount importance An advanced stenosis of the coronary orifices or arteries may exist with no abnormal findings Therefore knowledge of the typical subjective complaints is necessary and a detailed history must be obtained The statement so often recorded on charts — patient has anginal pain or pain in the precordial area — does not suffice

The pain is definitely related to effort At first it may occur only on great effort such as climbing several flights of stairs running after a train or walking uphill However sooner or later even walking on level ground induces the distress Commonly the pain is located in a very characteristic manner behind the sternum It may spread to the left or right chest to the left or right side of the neck the shoulder or the arm If severe it may reach the jaw or the ulnar aspect of the left or right hand In unusual cases it spreads downward and then radiates more often to the upper right side than to the left side of the abdomen Sometimes the retrosternal pain is absent and in its place there is only pain in the left elbow or hand or even the jaw Very rarely the distress may extend into the left leg down to the knee

The pain is usually described as a viselike constriction or a choking compressing sensation

Not uncommonly the presence of pain is denied a sensation of choking pressure or burning may exist or the patient may even disclaim these sensations to complain merely of a weakness of one or both arms As in coronary thrombosis painful sensations may be absent despite coronary stenosis and the intensity of pain permits no conclusion with respect either to the extent of the lesion or to the prognosis

The pain may force the patient to stop walking or working If this is done the typical pain subsides in a few minutes If the patient resumes walking the distress may recur but occasionally it does not return even if the walk is prolonged rarely the pain disappears even when the patient does not stop an observation noted by Heberden The patient walks off the pain

This is explained in the same way as the pain experienced by young healthy people at the beginning of strenuous exercise (mountain climbing cycling rowing) The coronary circulation does not adapt itself immediately to the increased demands from exercise and a myocardial hypoxia appears in the first minutes of physical activity With adequate dilatation of the coronary arteries due to reflexes and action of local metabolites an increased blood supply to the myocardium is obtained in the following minutes the pain disappears and the patient gets his ' second wind This mechanism also explains the common phenomenon that walking in the morning elicits the pain quickly while walking much longer distances later in the day fails to elicit unpleasant sensations (first effort pain)

It is also typical for these patients to note no pain when walking in their apartment or building for a long time walking one block in the open air elicits it

Exertional pain appears more often and with greater regularity and in some patients even exclusively if they walk after a meal or if they walk in cold and windy weather After a heavy meal the cardiac output increases almost 50 per cent this higher level is maintained for one to three hours (Grollman) If patients take a postprandial walk the work of the heart is further increased and the demands for blood may become sufficiently large to cause ischemia of the heart muscle if coronary stenosis is present The exercise tolerance of patients with angina pectoris following a meal is reduced on the average 25 per cent (Wayne and Graybiel) Walking against the wind increases work the cardiac output is also increased when cold air is blown on the skin of an experimental animal Cold leads to an increased output of adrenalin

In some cases anginal pain appears at the beginning of a meal and even when the patient swallows In this instance reflexes from the lower esophagus and stomach are obviously responsible as discussed before A similar mechanism may explain attacks appearing at rest and disappearing with the eructation of gas or the passage of flatus Experimental distention of the abdomen by gas also causes a reflex coronary vasoconstriction (Gilbert et al)

Anginal pain also appears on excitement Under these conditions the output of adrenalin may increase the blood pressure and heart rate and precipitate the pain (Raab)

Thus in coronary stenosis any mental or physical strain anything that increases the work of the heart and therefore its need for oxygen causes pain Great apprehension and anxiety (fear of impending death) often accompany the pain The mechanism responsible for this anxiety is unknown

SIGNS

Physical examination discloses no signs characteristic for angina pectoris due to coronary stenosis The physical findings are often normal This was stressed in the discussion of coronary sclerosis and it will be mentioned again in regard to luetic stenosis of the coronary orifices and aortitis Many surveys reveal that approximately 20 per cent of patients with exertional angina yield normal physical findings including x ray and electrocardiograms Therefore reliance must be placed mainly on the history

Many patients however do have abnormal findings An elevated systolic and diastolic blood pressure a dilated aorta an abnormally accentuated second aortic sound a rough systolic apical or aortic murmur caused by an athero sclerotic thickening of the mitral or aortic valves may be present The electro cardiogram may show T wave changes or wide slurred and notched QRS com plexes While these findings may aid in a doubtful case because they show that myocardial involvement is present they do not conclusively prove that a coronary artery stenosis exists and is the cause of anginal pain

The desire to obtain compensation the information obtained from news papers or from friends who suffer from angina pectoris may influence the history on which the physician relies for the diagnosis This coupled with the fact

that pain on effort occasionally occurs in conditions other than coronary stenosis makes understandable the desire to confirm the diagnosis by objective findings

Such confirmation is possible if the electrocardiogram is taken after exertion (Scherf et al)

Exercise Test At rest these patients often have a normal electrocardiogram despite marked coronary stenosis since the blood supply to the heart may still be adequate For the same reason they offer no symptoms or abnormal signs at rest On exertion however the oxygen requirements of the heart muscle increase but a larger blood supply to some areas is impossible owing to the existing stenosis Therefore pain as well as electrocardiographic changes may appear after exertion

Alterations in the electrocardiogram after effort have been known to occur in patients with angina pectoris (Wood and Wolferth) This procedure however was not recommended as a diagnostic test because the clinical observations are more likely to be significant from a diagnostic standpoint than the electro cardiographic phenomena Since the physical findings are often negative and — if present — are by no means typical the study of the electrocardiogram following exercise has been recommended in order to diagnose coronary stenosis (Goldhammer and Scherf)

The changes which appear after exercise in coronary stenosis consist of an abnormal depression of the RS T segment and the disappearance or inversion of the T waves in leads I and II and the precordial leads V 4 6 Great caution must be used not to confuse normal changes which appear in the electrocardiogram after physical exertion with those due to coronary stenosis The error committed most frequently is to declare a physiologic depression of the RS T segment after exercise to be pathologic Thus many normal postexercise electrocardiograms are called abnormal (false positive tests) In order to avoid this one should never interpret a depression of the RS T segment of less than 2 mm as abnormal The T of the P wave is markedly depressed after exercise and because of its long duration it depresses the RS T segment so that the reference point for the evaluation of the position of the RS T segment should be the position of the string at the beginning of the QRS complex and not the zero line The changes described above as pathologic are not observed in healthy subjects after light or even after strenuous exercise Only after unusual strain (e g

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FIG 81 The electrocardiogram of a patient with coronary stenosis caused by athero sclerosis and angina on effort before (a) and after (b c d) exercise

FIG 82 The three standard leads are followed by V 2 and V 5 The tracings were obtained from a 65 year old man with angina on effort due to coronary sclerosis At rest (a) the T waves are low but positive Two minutes after exercise (b) there is a borderline depression of the RS T segments and atrial extrasystoles appear (V 2 and V 5) Six minutes later (c) there is a definite inversion of the T waves which are abnormal fifteen minutes after the exercise (d) the T waves are higher than prior to undertaking the exercise This is a common phenomenon (Scherf and Goldhammer)

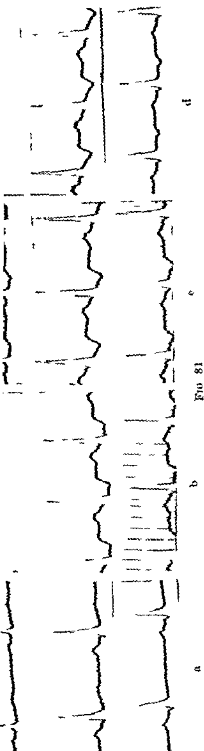


FIG 81

FIG 82

marathon running) have similar changes been reported as a rare occurrence in the normal heart Patients without coronary stenosis (myocardial or other types of heart lesions) likewise do not show the changes mentioned They are characteristic of coronary stenosis They have been observed in myocarditis although rarely

The series in figure 81 was obtained from a 56 year old man with coronary stenosis and angina on effort Physical examination gave normal results The first tracing (figure 81a) was taken at rest and shows only low T waves in the three limb leads The second tracing taken immediately after the patient walked up and down two flights of stairs shows depression of the RS T segments and of the T waves (figure 81b) In figure 81c and figure 81d recorded five and ten minutes after the exercise the changes are still very marked although the exercise had stopped

If patients are asked to do no more exercise than they perform repeatedly during their daily occupation this test involves no risk In some cases the exercise test is normal before but positive after a meal The test shows abnormal changes in 80 per cent of patients with coronary stenosis The alterations are independent of the presence of pain and depend solely upon the amount of the coronary blood flow They are sometimes absent if nitroglycerin or theophylline are given immediately before the test is done The changes in the electrocardiogram sometimes persist for 50 minutes after the exercise and therefore are scarcely the result of hypoxia alone (Scherf 1935)

Figure 82a shows the three standard leads as well as the leads V2 and V5 from a 65 year old man with angina on effort The only abnormality consists in low T waves in all leads The electrocardiogram obtained immediately after exercise (figure 82b) shows a depression of the RS T segment which is borderline An inversion of the T waves followed in figure 82c which was registered 6 minutes after the exercise In figure 82d obtained 15 minutes after the exercise the electrocardiogram is again normal Actually the T waves are higher than before the exercise which is a common phenomenon (Scherf)

We are opposed to Master s modification of the test since we do not think that the amount of work performed by the patient should depend upon the age sex and weight The condition of the coronary artery should dictate the amount of work as we originally recommended Work undertaken in accord with Master s tables is too much for one and too little for the second patient This is why work must be done twice or three times (double treble tests) But then we are no longer dealing with a standard test Since a given amount of work will mean a different load for the heart whether the work is done by a person in good or bad physical training before or after a meal slow or fast relaxed or with tension a standard' performance is from the beginning impossible

Anoxemia Test The tests in which hypoxemia is produced by breathing from a bag (Rothschild and Kissin) or by breathing a mixture containing reduced amounts of oxygen (Dietrich and Schwiegk) have the disadvantage of requiring additional apparatus Also they are less useful because abnormal changes are

occasionally seen in healthy subjects in anemia and in other conditions (Larsen) they are not specific for coronary stenosis

Ballistocardiogram Even in patients who do not show any abnormality in the electrocardiogram and who exhibit normal clinical findings the ballisto cardiogram may reveal abnormalities An early M form appears the I wave becomes smaller or the J wave is M shaped The waves are abnormally low and abnormal respiratory changes appear However patients with typical angina pectoris may have a normal ballistocardiogram Probably it is abnormal only in those who have small necroses and fibroses Results must be evaluated with caution Thus one must keep in mind that an abnormal ballistocardiogram is found in only 80 per cent of patients with a healed myocardial infarction

DIFFERENTIAL DIAGNOSIS

The differential diagnosis between angina pectoris due to coronary stenosis and the pain of coronary occlusion usually is easy The tables used in older books in order to illustrate this are therefore unnecessary today In coronary stenosis pain typically follows the provocative factors mentioned previously whereas in coronary thrombosis the pain appears without visible cause In coronary stenosis the patient soon learns the relation between certain acts and the pain and tries to avoid precipitating an attack In coronary occlusion the pain usually lasts for hours certainly longer than a few minutes In angina on effort due to coronary stenosis the pain disappears quickly if the patient stops walking or if the reason for the excitement passes One may safely state that whenever the pain lasts longer than five minutes a simple uncomplicated coronary stenosis is no longer responsible The pain in coronary stenosis is regularly relieved by nitrites which do not help in coronary occlusion

The benefit afforded by nitroglycerin in coronary stenosis is so regular that this fact is utilized with great advantage as a therapeutic test Whenever the history is atypical or unreliable it is advisable to administer one tablet of nitroglycerin during the pain If this brings relief within one minute anginal pain is most probably present One must make sure that relief comes within a minute since patients often state that nitroglycerin helped even though further inquiry reveals that five or six minutes were required for the pain to vanish The effect of nitroglycerin is prompt and remarkable even with marked luetic narrowing of the coronary ostia in which instances an increase of blood flow in the coronary arteries due to the drug is impossible It is believed that an increased capillarization the widening of the peripheral sections of the coronary tree helps in these instances An antiadrenergic effect of nitroglycerin has been assumed to exist (Raab and Lepeschkin) The tablets used for this test must be fresh since nitroglycerin deteriorates with time

Apart from the above mentioned characteristics some negative evidence also aids in ruling out coronary occlusion Thus fever leukocytosis and fall of blood pressure are absent in simple coronary stenosis

If patients state that their attacks are increasing in frequency and that the episodes tend to occur more often during rest, that they are becoming more prolonged or that nitrites are less effective, the danger of an occlusion is imminent. As pointed out earlier, in some cases of coronary thrombosis, pain lasting from five to fifteen minutes occurs at rest for a few days before the attack.

In spondylarthritis, in cardiac neurosis and in hiatus hernia, it is occasionally reported that pain occurs on exertion, after meals or excitement, but careful interrogation discloses that there is not always an immediate and direct relation between the alleged releasing factor and the pain; moreover, in neurosis the pain is too brief (stabbing) or too long to permit the diagnosis of coronary stenosis. In spondylarthritis, the pain is often elicited by a certain posture and in hiatus hernia belching brings relief. The latter phenomenon, however, often also appears in true angina due to coronary stenosis.

We have had the opportunity to observe a patient who complained of pain only while lying on his left side. Physical examination gave negative results but the T wave in lead I was low. The patient was put to bed and died suddenly five days later when he turned to his left side on the order of his nurse.

It is particularly important to obtain a very careful history when the examination reveals no abnormal findings. Sometimes, especially at the beginning when an abnormal sensation has appeared but once or twice, a differential diagnosis is difficult or impossible. Some of these patients turn out to have only a harmless spondylarthritis or fibrositis, while others soon develop a coronary thrombosis and may die a few hours after the examination which did not reveal any abnormal findings. Therefore, great caution must be exercised before making a diagnosis as ominous as coronary artery disease or before the patient is dismissed as suffering from a harmless condition.

Decubitus Angina. A small percentage of patients with coronary stenosis have their attacks of angina at rest, particularly at night, for months and years (decubital angina). This type is associated in most instances with a remarkable rise of blood pressure in the attack. The hypertension is often attributed to an exciting dream, but usually there is no apparent cause. This type of anginal pain will be discussed at greater length in the chapter on hypertensive crises.

Even if the history of pain is atypical, a positive result of an exercise test or the presence of abnormal findings such as aortitis, hypertension, or cardiac enlargement should make the physician strongly suspect coronary disease.

CLINICAL COURSE AND PROGNOSIS

It is extremely difficult to predict the course of the disease and to prognosticate its duration. A patient with a moderate exertional angina due to coronary sclerosis may show no further change for many years. One of us saw a patient with an angina on effort in whom the attacks were unchanged over a period of 24 years. The process may be arrested at any stage. Luetic stenosis of the coronary ostia has a poorer prognosis, since progression is typical for this lesion

In these patients as in all other coronary artery diseases sudden death may occur at any time While patients with many attacks on the least provocation are in greater danger than those who develop distress only after severe strain such as climbing stairs after a heavy meal accidents happen in both groups

Attacks of angina pectoris may disappear This happens if a narrowed coronary artery becomes occluded by an acute thrombosis or if a slow fibrotic occlusion occurs without the acute signs a of myocardial infarction If the other main coronary vessels are patent and the blood supply to the heart is sufficient on exertion as well as at rest the patient may feel perfectly well for years Anginal pain often disappears with the onset of fibrillation or congestive heart failure In our experience this occurs particularly in groups of patients with angina on effort as a consequence of syphilitic coronary stenosis when the liver enlarges or edema appears if digitalis successfully controls these symptoms the angina recurs although there is no change in physical activity during the interim This phenomenon has not been satisfactorily explained although it has been known to clinicians for a long time

The intensity of the pain on effort has no prognostic significance the electrocardiogram may show marked hypoxia of the heart muscle without much pain in the attack or the pain may be severe while the electrocardiogram shows only trifling changes

Obviously the patient should always be encouraged as to the outlook however in discussing the situation with relatives the physician should not neglect to mention the possibility of accidents that may occur at any time

Therapy

General Management It is vitally important in the treatment of angina due to coronary stenosis to reassure the patient The term angina pectoris should not be used in his presence Nowadays every patient knows the ominous significance of this diagnosis If the pain is explained as a vascular spasm or a disturbance of the cardiac arteries which prevents a normal blood supply to the heart the patient accepts this with much less alarm than the diagnosis of angina pectoris

The patient must avoid as far as possible all factors that tend to precipitate an attack He must avoid great exertion such as is inevitable in climbing stairs or hills Often walking on the level produces no pain whereas walking up a very slight incline immediately releases it An attempt must be made to avoid undue excitement and the patient should have frequent but small meals Protection against cold is important and it is wise to avoid walking against the wind If these rules are observed by a simple alteration of the mode of living and without other therapy one occasionally succeeds in rendering the patient free from attacks

Treatment of Coronary Artery Disease Unfortunately very little can be done to influence the underlying basic illness in angina on effort syphilitic

aortitis or atherosclerosis In aortitis leading to coronary stenosis and angina on effort specific therapy will be of little avail The disease is however less common in recent years It will be discussed in a later chapter

In atherosclerosis all measures hitherto recommended are of dubious value Choline seemed to help in experimental atherosclerosis but this was not confirmed the same holds for methionine and inositol There is no sound basis for the use of these compounds The effect of the commercially available capsules containing unsaturated fatty acids with nicotinic acid and pyridoxin is still under investigation While experimentally the estrogens reduce the degree of atherosclerosis in chicks there is no justification as yet for the therapeutic use of these substances in man because of the side effects

Heparin was found to clear the lipemic plasma and it was recommended to treat coronary atherosclerosis by injections of 50—100 mg of heparin once or twice weekly Fantastic results have been reported but not confirmed

Usually weight loss should be advised Following a marked loss of weight *a significant decrease of serum Sf 12—20 lipids was observed* (Walker et al) A fat poor and cholesterol poor diet is recommended No cream soups glandular organs tongue fish roe cake fried food cream or butter are permitted Cheese may be eaten only if made from skimmed milk At the most two eggs per week are permitted No nuts or avocados are allowed Not more than 25 grams of fat and 75 mg of cholesterol should be ingested per diem While thyroid hormone diminishes the cholesterol content of the blood rarely can it be given to these patients for reasons that are obvious

Bed Rest There is no rationale for continuous rest in bed Often we see patients who were advised to go to bed for four weeks or more because of their angina on effort When they get up the old complaints are present as before The tolerance to exercise is not increased by bed rest When patients live under great strain separation from the sources of anxiety will help

Nitroglycerin The best remedy in an attack is nitroglycerin It is far better than amyl nitrite which has been prescribed since Sir Lauder Brunton s recommendation Not only does amyl nitrite cause a disagreeable odor in the room but the marked cardiac acceleration and the decided fall of blood pressure induced by it are disadvantageous The tachycardia may increase the oxygen requirements of the heart without the possibility of providing an adequate supply so that more pain and marked electrocardiographic alterations result

One starts with the smallest available dose of nitroglycerin usually 1/200 gr in the form of the easily soluble hypodermic tablets The pharmacist must provide the patient with a fresh preparation which should be stored in a glass bottle or vial it deteriorates readily and loses strength if exposed to air

If the administration is associated with pronounced untoward *symptoms such as flushes dizziness headache and the like the patient may take half* a tablet In this way the dosage is more easily adapted to the needs of the patient In rare cases sweating syncope and other symptoms are provoked by a sudden drop of blood pressure following the administration of one tablet of nitroglycerin

It is therefore advisable to have the patient take his first tablet while at home in bed in order to familiarize himself with its action In very rare cases nitroglycerin aggravates the pain

Some patients are afraid to take nitroglycerin freely This fear is based partly on a misconception arising from the name of the compound and partly because it helps so much that patients are afraid its effect will wear off and will not be available when needed It is well to point out that the untoward reactions disappear if the remedy is used more often while the therapeutic effect remains Moreover there is no danger of a diminished response for the average case if the remedy is taken often It should *always* be within reach of the patient and be taken whenever needed Even if the patient is in doubt whether a particular pain is due to his heart or is of different origin a tablet should be taken Not rarely physicians advise the patient to take tablets only when the pain is severe this is positively incorrect It is better to take 10 tablets too many than one too few Tablets of nitroglycerin need not be put under the tongue keeping them in the mouth will suffice to obtain a satisfactory effect

Of great importance is the prophylactic use of nitroglycerin which was recommended by Murrell and subsequently by others If ascending an unavoidable flight of stairs or walking up a sloping street regularly induces pain the patient should prevent an attack by taking a tablet of nitroglycerin about a minute before the pain is expected In a similar way nitroglycerin should be taken for preventive purposes before business meetings conferences sexual intercourse etc in order to avoid the anginal pain caused by excitement This advice may make most patients cooperate and may free them from distress despite a continuation of their activity Concerning this prophylactic treatment with nitroglycerin it should be remembered that the prophylactic action rarely lasts longer than 10 minutes

Treatment with nitroglycerin in small doses (1/200 gr) given every two to four hours may help patients with many attacks of angina pectoris at rest

We are very satisfied with the slowly absorbable nitroglycerin preparations (Nitroglyn gr 1/10 or 1/25 1 tablet every 12 hours) In some patients headache appears and they are told to take 3/4 or 1/2 a tablet morning and night In more than 60 per cent of the patients much less nitroglycerin is necessary while these tablets are taken since less pain is experienced In order to avoid tolerance this medication is interrupted for one week every 4 or 5 weeks

Other Vasodilators The value of other drugs in angina pectoris due to coronary stenosis is a disputed issue Empirically and on the basis of animal experiments several drugs have been advised for dilating the coronary vascular tree as much as possible thereby enhancing the formation of a collateral circulation

There have been a few series of carefully controlled investigations on ambulatory patients who suffered from angina on effort These patients received different drugs recommended for this condition as well as a placebo The same percentage of improvement was found in those taking the various drugs as

in those who were treated with a placebo (Evans and Hoyle) This result is the basis for the great pessimism that prevails with respect to the possibility of influencing the course of the disease or the condition of the patient by means of vasodilators many physicians stopped prescribing anything but nitroglycerin to patients with angina on effort

We are personally convinced that treatment with coronary vasodilators is useful We have often seen patients ask for a certain prescription because they felt better as long as it was taken It is equally true that certain patients fail to respond to all forms of therapy for the process in the coronary arteries is too advanced Nevertheless every patient deserves the benefit of a trial

It is often stated that vasodilators cannot help in cases with advanced coronary sclerosis because the arteries are too profoundly altered The following observation argues against this point At autopsy we repeatedly found the orifices of both coronary arteries almost completely occluded by a syphilitic process although the coronary arteries themselves could not admit a larger amount of blood nevertheless nitroglycerin aided greatly during the anginal attacks of the patient The dilatation of the extracardiac and intracardiac anastomoses of the coronary system or an unknown specific action of nitroglycerin (Raab and Lepeschkin) may cause this improvement One may therefore assume that the vasodilators help even in extreme coronary narrowing

Among the compounds related to nitroglycerin erythrol tetranitrate is the best for prolonged and regular administration Its chief drawback is the headache which often occurs even if small tablets (0 005 Gm) are taken three times a day Accordingly not more than 0 003 Gm should be given as a single dose The advantage of erythrol tetranitrate consists in its more prolonged action perhaps the result of slower absorption

Headaches also follow the administration of mannitol hexanitrate in a dose of 0 06 Gm three times daily We have not observed any improvement from penta erythrol tetranitrate (Peritrate) and dioxelene phosphate (Paraveril phosphate)

Purine bodies such as theobromine sodium salicylate (Diuretin) pure theobromine theobromine calcium salicylate (theocalcin) and particularly theophylline have been used as coronary dilators for many years A stimulating effect on cardiac contraction is combined with definite coronary dilatation Pure theophylline often irritates the stomach and produces nausea In combination with ethylenediamine which acts as a solvent theophylline is tolerated better the new drug is called aminophylline (euphyllin metaphyllin) and is given in tablets of 0 2 Gm three times a day The enteric coated tablets are tolerated much better but their absorption is slower Our experience with the latter type of tablet is much more satisfactory than with plain tablets

A preferable method of administering aminophylline because of more pronounced effect is by rectal suppositories We give 0 5 Gm of the product in each suppository and advise the patient to insert one or two suppositories daily Sometimes the administration of 0 5 Gm of theophylline ethlendiamine

(aminophylline) in 30 ml of water as a retention enema is more rapid and more complete Rarely intolerance to the drug is encountered This is manifested by excitement irritability headache or local rectal irritation These events are exceptional as a rule the remedy is well tolerated

Strongest vasodilatation is accomplished by the intravenous use of theophylline The injection of theophylline ethylenediamine must be done very slowly to avoid marked vasodilatation with vertigo and fall of blood pressure The injection should take at least five minutes and it may be repeated daily in the same amount

If an intravenous injection comes under consideration we prefer the soluble theophylline sodium acetate This salt is tolerated much better and does not cause untoward reactions Usually a 5 per cent solution is employed and 5 ml are given as the first dose This amount may be increased by 1 ml daily until the full dose of 10 ml (0 5 Gm of theophylline sodium acetate) is given with each injection In a very small fraction of the cases a sensation of irritability and excitement may limit the physician to giving no more than 5—6 ml daily A total of 12 to 15 injections constitutes a series With these injections more is accomplished than with any other therapeutic procedure as the coronary dilating effect is pronounced unfortunately improvement often lasts only for the period of administration of the drug

It has been possible to show the therapeutic value of theophylline objectively the electrocardiographic alterations appearing regularly after exertion fail to develop if the same exercise is repeated shortly after an intravenous injection of the drug (Scherf)

The administration of papaverine hydrochloride 0 05 Gm by mouth or 0 02—0 04 Gm intravenously has often been recommended There is no doubt that papaverine is a powerful coronary vasodilator and it should be used more frequently but its price is often prohibitive and in our experience theophylline injections have a better and a more prolonged effect

Atropine has been frequently mentioned as a useful drug for angina pectoris and formerly was often prescribed Since the vagus acts as a constrictor of the coronary arteries and the tonic innervation permits a maximal coronary blood flow only after atropinization some result should be expected On the other hand the amount of atropine permissible is one which does not appreciably affect the heart rate

Since large and effective quantities of all these remedies cannot be given over a long period it seems best to proceed in a manner that allows a combination of several agents having partly different points of action Although this combination recalls the polypharmacy of former times results are obtained with this combination that are not approximated by the use of single ingredient We cannot understand why the administration of these drugs in a mixture made in the pharmacy should do harm while the simultaneous ingestion of the same ingredients from different bottles should be useful

The prescription is as follows

	Gm
Erythrol tetranitrate	0 003
Papaverine hydrochloride	0 05
Phenobarbital	0 01
Atropine sulfate	0 0002
Quinidine sulfate	0 1
Acetphenetidin	0 1
Theobromine pure	0 15—0 20

The relatively small dose of erythrol tetranitrate does not cause headache phenobarbital is a central sedative and acetphenetidin advocated already by Huchard is an analgesic In the dose prescribed atropine accomplishes no more than a reduction of vagal tonus Quinidine is a powerful vasodilator and a depressant of the tonus of the autonomic nerves

From this mixture one capsule is prepared such capsules are given three times a day one after each meal Rarely hypersensitivity to phenobarbital quinidine or theobromine is encountered and these drugs must then be omitted from the mixture The capsules are given for 3 to 4 weeks and in many cases there is a definite improvement with regard to the severity frequency and duration of the attacks Naturally refractory cases are encountered since all therapy is ineffective when alterations are advanced Occasionally the symptoms recur if the capsule is stopped under these circumstances there is no objection to another course of administration

The occurrence of spontaneous improvement in patients with coronary stenosis compels one to exercise caution in the appraisal of all therapeutic measures With the capsules just mentioned with nitroglyn with aminophylline suppositories and with intravenous injections of theophylline we possess a powerful therapeutic armamentarium to improve the patient s condition and we have a real basis for hope and encouragement although we cannot alter the course of the disease or influence the dubious outcome

Administration of pressor amines should be avoided Parenteral therapy with Priscoline and Pitressin may lead to severe attacks of angina pectoris

Khellin Promising results have been obtained with khellin preparations obtained from ammi visnaga a wild plant from the Eastern Mediterranean Used widely in Egypt for the treatment of kidney stones and bronchial asthma it has a coronary vasodilating effect that surpasses that of papaverine and aminophylline as was demonstrated by Anrep and his co workers In those patients who tolerate the drug good effects may be obtained we do not agree with those who claim that khellin is of doubtful value In several of our patients the complaints recurred a few days after the drug was withdrawn The dosage is different with different preparations on the market One gives advisedly the smallest dose of a preparation which is on the market once daily and gradually increases the number of tablets to as many as are tolerated Unfortunately side effects

such as severe nausea vomiting diarrhea excitation or abnormal sedation weakness confusion depression and fever appear in about 60 per cent of those who take the drug

Propylthiouracil Radioactive Iodine Surgical thyroidectomy is now abandoned in favor of the chemical blocking of the formation of thyroid hormone with propylthiouracil or similar compounds or with radioactive iodine This therapy sponsored mostly by Raab and Blumgart brings a slow improvement since all thyroxin already formed by the gland must be first exhausted a process which may require weeks Patients with angina pectoris seem to do best with a basal metabolic rate of minus 15—25 per cent Clinical observation is a better guide One administers 25—150 millicuries of radioactive iodine in three divided doses Against the objection of a possibility of enhancement of atherosclerosis by the myxedematous state Blumgart has emphasized that in a very limited number of subjects who were examined at necropsy years after thyroidectomy no evidence of advanced coronary sclerosis was observed

Tobacco Smoking should be discontinued Although there is no proof that smoking alone causes coronary sclerosis it is equally indisputable that the angina pectoris of coronary stenosis may be aggravated by smoking It is a common observation that heavy smoking in healthy youngsters causes precordial pain which gradually disappears if the smoking is discontinued Tobacco angina is however rare In patients with and without organic heart disease temporary changes in the electrocardiogram have been observed following smoking of a single cigarette Patients with angina pectoris may improve when they stop smoking Whether the detrimental effect of smoking is due to vaso constriction or the increase of heart rate and blood pressure is not decided

In young men angina pectoris seems to occur more often among heavy smokers than non smokers In elderly people no differences were observed in the incidence between both groups

Methonium We lack experience in the therapy of angina pectoris in hyper tensives with methonium Doyle and Kilpatrick treated 50 patients As to be expected spontaneous pains appeared in some and the treatment had to be terminated Many patients however showed improvement and in one third anginal pain disappeared We saw improvement with rauwolfia

Alcohol The moderate use of alcohol is permissible indeed it had been regarded as a beneficial agent owing to its vasodilating effect and was recommend ed by Heberden There is no proof that alcohol dilates the coronary arteries Beer and champagne like other carbonated drinks should be avoided because of the resulting elevation of the diaphragm which is not well tolerated

Spa Treatment Spending a few weeks at a health resort has the advantage of rest and relaxation but it has the disadvantage that the patient may learn too much about the symptoms and complications of his disease from fellow patients Naturally it is beneficial to spend the winter in a southern climate however while this adds to the well being of the patient he should be informed that this will not cure his condition

Irradiation of Adrenals Starting from the theory that attacks of angina pectoris in cases of coronary stenosis occur after physical exertion exposure to cold weather or emotional factors – conditions in which according to Cannon large amounts of adrenalin are discharged from the adrenal medulla – irradiation of the adrenals with roentgen rays has been recommended (Raab) Six single treatments are given on consecutive days Three treatments are applied to the left side and three to the right each side being treated on alternate days Two hundred roentgen units are given at each treatment The size of the field is 15 × 15 cm 200 kv 20 ma 50 cm target skin distances 1 5 mm Cu plus 1 0 mm Al filter

In more than 20 personally observed cases the results were satisfactory and seemed to go definitely beyond the individual variations in the course of the disease and psychic effects inherent in any therapeutic procedure

Surgery When the attacks cannot be controlled medically and occur with such frequency that life is intolerable to the patient surgical measures may bring relief Some patients suffer such agony that they are willing to undergo any surgical intervention which promises help

Candidates for any surgical procedure must be carefully selected and one fact should be constantly kept in mind namely that spontaneous improvement may occur at any time irrespective of the intensity of subjective sensations or objective findings The surgical procedures may be divided into three groups

(1) Operations aimed at interrupting pain fibers on their way to the centers This is a purely symptomatic measure without influence on the pathologic process

(2) Thyroidectomy which does not influence coronary blood supply directly

(3) Operative procedures designed to increase the blood supply to the heart by creating anastomoses

INTERRUPTION OF PAIN FIBERS Since Francois Franck s demonstration that sensory fibers from the heart pass over the sympathetics operations on the cervical and dorsal sympathetics have been recommended Many of the original procedures proved useless or were not compatible with anatomic facts The mortality was over 10 per cent Extirpation of the stellate ganglion afforded relief in a fair number of cases although sensory fibers also run from the heart directly to the upper thoracic ganglia Extirpation of these ganglia bilaterally and section of the upper five dorsal roots are very formidable operations No improvement is obtained in 8 per cent of the patients Intercostal neuralgia appears in 10 per cent Pleural effusion radiculitis and even transverse myelitis have been reported Therefore paravertebral anesthesia with a mixture of novocaine and alcohol is preferred at present When done by a competent physician the risk of complications is small and the percentage of patients benefited is great However in over 50 per cent neuritic complaints result which may be very troublesome Relief from the angina may last for a month or it may be permanent Instead of pain patients receive other warning signals such as sensations in the jaw behind the sternum or choking

TOTAL THYROIDECTOMY This has been abandoned since the advent of the thiourea drugs and radioactive iodine which were discussed above

OPERATIONS FOR INCREASING THE BLOOD SUPPLY TO THE HEART Opinions about the value of operations intended to increase the blood supply of the heart by creating anastomoses with the extracardiac circulation are divided A definite indication for such an operation would be the progressive narrowing of the coronary ostia by syphilis This condition can be diagnosed clinically and since all other therapeutic procedures are useless an operation may be justified once the diagnosis is established In patients with coronary sclerosis we hesitate to advise surgery When attacks increase in intensity and occur more frequently even at rest often a coronary occlusion threatens Therefore the mortality of these operations is so high signs of a myocardial infarction appear often during surgery or immediately afterward

Among the operations reported there are several which have become well known Grafting a part of the left pectoralis muscle on the heart grafting omentum on the exposed heart (cardio omentopexy) and the creation of pericardial adhesions by talcum powder (cardiopericardiopexy) (Thompson) or by bone dust (Beck) represent the chief methods recommended Vein grafts between the systemic arteries and the coronary sinus veins were performed (Beck et al) Creation of this type of arteriovenous fistula is attended by a high mortality The De epicardialization operation with a 95 per cent phenol solution (Harken et al) seems promising No proof has been given that following a surgically induced pericarditis sufficient anastomoses form between pericardial and coronary vessels

Even implantation of mammary arteries into the left ventricular myocardium (Vineberg) occlusion of the coronary sinus vein and pericoronary neurectomy (Fauteux) have been recommended There is as yet too little experience available to evaluate the effect of the ligation of both mammary arteries in the second intercostal space

CORONARY INSUFFICIENCY (CORONARY FAILURE THE INTERMEDIATE SYNDROME) AND LITTLE INFARCTIONS

The fact that the currently fashionable diagnosis of coronary insufficiency indicates only a physiologic state and not a clinical entity has been stressed in the introduction to this chapter The term is widely used to indicate a great variety of conditions Danielopolu employed it early to indicate the occurrence of angina pectoris without coronary disease during strenuous exercise Physiologists then used it to describe a blood supply to the heart which does not fulfill the need i e the oxygen requirements Some of them spoke rather vaguely of a coronary insufficiency when there was an anemia or carbon monoxide intoxication Under these circumstances the coronary arteries are normal but the supply of oxygen to the heart alone suffers Great confusion was created subsequently Katz describes coronary thrombosis with myocardial infarction

under the heading of coronary insufficiency Master described necrosis or infarction of the heart muscle without complete occlusion of a coronary artery as coronary insufficiency and later interpreted this term to mean attacks of pain in between angina pectoris and myocardial infarction without or with very little fall of blood pressure elevation of the sedimentation rate and no QPS changes in the electrocardiogram Shock is rare Nitroglycerin helps little or not at all A similar syndrome was described by Freedberg et al as coronary failure and by Graybiel as the intermediate syndrome

In our opinion most of these patients have sustained *little infarctions* an extremely common but little recognized condition

A very odd situation prevails at the present time large classical infarctions are readily diagnosed while little infarctions (like the little strokes emphasized by Alvarez) are not recognized We have seen such infarctions occur repeatedly in some individuals over a period of years Contrary to the statements of some authors these little infarctions like the (larger) rudimentary infarctions of Holzmann may be accompanied by extremely severe pain which lasts for hours There may be a very slight rise of temperature but usually there is none at all The blood pressure remains unchanged or falls a little and only temporarily the sedimentation rate rarely becomes abnormal very often the electrocardiogram is normal since the lesion is intramural not reaching the subepicardial or subendocardial layers occasionally it shows flattening or a transient inversion of the T waves in some leads for the most part the V leads of the chest The tracings described by East and Oram belong here

The attacks are rarely caused by thrombosis of a coronary vessel Usually a fibrotic occlusion of a small tertiary branch is responsible (Wolkoff) The fibrotic occlusion of tertiary branches of the coronary arteries caused by coronary sclerosis is particularly common in hypertension It will not of course be prevented by the administration of anticoagulants It is in our opinion a frequent cause of little infarctions

The patient may have only one such attack if all findings are normal or if he remains healthy over a period of years the diagnosis of coronary disease is often not made In other patients such attacks occur almost daily for weeks or months and require repeated injections of morphine In some cases a series of such attacks leads to myocardial fibrosis without a large area of necrosis but causing heart failure There are countless variations of the clinical picture At any time the attacks may subside A large infarction may appear after years of well being

Such patients require rest only for a few days They may have bathroom privileges *Treatment is symptomatic*

In our opinion the diagnosis of coronary insufficiency coronary failure or intermediate syndrome (Graybiel) is less exact in these cases than the recognition that we are dealing with little infarctions caused by occlusion of small branches of the coronary arteries

The term coronary insufficiency is justified only with a qualification indicating a particular pathophysiologic state such as coronary insufficiency due to coronary stenosis (syphilitic) or paroxysmal tachycardia aortic stenosis acute hemorrhage and so forth We prefer however to speak of a myocardial hypoxia in these conditions — thus indicating the etiologic mechanism — rather than a coronary insufficiency

ANGINA PECTORIS DUE TO AORTIC AND MITRAL VALVE LESIONS

Anginal and precordial pain is not rare in rheumatic mitral lesions and in rheumatic or syphilitic aortic valve lesions Such cases frequently are appraised incorrectly because the radiation of the pain its constant appearance duration and occurrence at rest are atypical

Mitral Stenosis The association of this type of pain with mitral valve lesions especially when stenosis is preponderant has been known for a long time and different theories have been advanced to explain the relationship (p 197) Exertional pain is uncommon in this lesion since dyspnea prevents great exertion and difficult breathing together with palpitation dominate the picture If anginal pain appears at rest the electrocardiogram taken during the pain shows evidence of myocardial ischemia (Scherf and Goldhammer) There fore an insufficient blood supply to the heart must be assumed This might be caused by higher intraventricular pressure in the right ventricle which increases resistance in the peripheral coronary vascular tree The appearance of anginal pain in cor pulmonale (see later) makes it probable that some of these pains originate in the pulmonary artery when the pulmonary arterial pressure is in creased In favor of this assumption is the fact that successful mitral surgery causes this most annoying symptom to disappear

Aortic Stenosis In aortic stenosis a similar mechanism seems active to some extent in the left ventricle This lesion is associated with anginal pain more often than are mitral lesions because the patients are able to perform physical work without dyspnea even when the aortic stenosis is rather advanced In this lesion pain is also common during complete rest The electrocardiogram in these cases if taken during an attack of pain repeatedly shows the same alterations as in coronary stenosis (Scherf 1935) A suction effect exerted on the coronary ostia has also been held partly responsible for the causation of the pain It is more probable that the unusual hypertrophy of the left ventricle encountered in this lesion and the increased intraventricular systolic pressure lead to myocardial hypoxia

Sometimes in aortic stenosis pain recurs so frequently that the patient is unable to take more than a few steps without pain or is awakened nightly from sleep Since there is no dyspnea pain is the only complaint although this pain is so distressing that the morale of patients is shattered and they may contemplate suicide

Aortic Insufficiency In the presence of a syphilitic aortic insufficiency anginal pain is often due to a stenosis of the coronary ostia in the course of the aortitis Anginal pain occurs however in all types of aortic regurgitation without coronary involvement

The combination of aortic insufficiency and angina pectoris has been known for almost a century In some cases of aortic insufficiency of rheumatic or syphilitic origin the anginal pain is unusually severe although the coronary arteries are normal this is not rare in children and young adults or in older patients This anginal pain was found to occur in 8 per cent of patients presenting aortic insufficiency (Laplace) The pain has been explained by the low diastolic blood pressure (White and Mudd) an explanation which seemed logical when the coronary blood supply was believed to depend exclusively on the height of the blood pressure the fact that the attacks occurred mostly at night was explained by the particularly low blood pressure levels existing at that time On the other hand patients with aortic insufficiency and very low diastolic blood pressure have no more attacks than those with somewhat higher pressures (Laplace) Furthermore it is easy to find that the blood pressure values during the attack are far from low In our opinion patients with aortic insufficiency and angina pectoris in the absence of a syphilitic stenosis of the coronary ostia belong to a group discussed in the next section — patients with hypertensive crises In the same group may be placed some patients with aortic stenosis and anginal pain

Treatment Nitroglycerin invariably gives relief from the anginal pain in all these patients with mitral and aortic lesions Our measures for preventing the recurrence of attacks are limited We have noted beneficial effects from theophylline given intravenously This alone may procure a restful night without anginal pain particularly when the injection is given in the evening The relief is only temporary however and recurrences tend to follow the discontinuance of injections In some cases rectal suppositories of aminophylline in a dose of 0 5 Gm help if they are inserted in the evening The oral administration of aminophylline is useless

These patients are often willing to undertake any treatment suggested by physicians to obtain relief surgical intervention may be indicated One of our patients secured immediate and lasting relief by total thyroidectomy Chemical thyroidectomy with thiouracil is of great help (Scherf and Terranova) Further therapeutic measures will be discussed in the following section

ANGINA PECTORIS IN HYPERTENSIVE CRISES

Since the classical description by Pal paroxysmal and transient rise of blood pressure is called a hypertensive crisis Such crises occur in a variety of conditions Pal described them in acute nephritis in the toxemias of pregnancy uremia and in lead poisoning We shall limit the description of hypertensive crises to the types encountered in cardiovascular disorders We are dealing

with a rather well known clinical syndrome which is often associated with angina pectoris Hypertensive crisis associated with pheochromocytoma will be discussed in the section on hypertension

Hypertensive Crises in the Absence of Pheochromocytoma

For many years it has been known that the blood pressure rises during an attack of angina pectoris This increase is so regular that Pal called angina pectoris an angiospastic crisis In more than 100 cases the blood pressure was regularly taken by one of us during an attack of anginal pain appearing at rest and the rise of blood pressure (which involved both the systolic and diastolic pressures) was never missed in decubital angina with the exception of certain special cases (attacks due to paroxysmal tachycardia pulmonary embolism etc)

Incidence Attacks of paroxysmal hypertension with anginal pain are very common in patients with aortic insufficiency at any age including childhood The same syndrome occurs in aortic stenosis aortitis moderate hypertension coronary sclerosis and occasionally in women with climacteric symptoms

Symptoms and Signs The symptoms closely approximate those observed in patients with a pheochromocytoma The patients suddenly and unexpectedly develop palpitation with some oppression which often develops into agonizing retrosternal pain with the typical radiations noted in angina pectoris There is profuse perspiration and the initial pallor is followed by a strong facial flush The systolic pressure often rises more than 100 per cent and values over 300 mm Hg are frequently recorded during the attack even when the systolic blood pressure does not exceed 130 mm Hg in the interval The diastolic blood pressure also rises but rarely more than 20—40 mm Hg Sometimes the anginal pain is absent and an unusually severe headache is present

A 14 year old boy had a slight insufficiency of the aortic valve after rheumatic fever He developed severe headache for many weeks and the distress recurred every afternoon at about five o clock The blood pressure values were always found around 110/40 except during the attack when they rose to 220/70 The episodes disappeared suddenly without treatment and did not recur (Scherf 1935) There was no decompensation A similar severe headache with paroxysmal hypertension and no anginal pain was observed by one of us in a patient with coarctation of the aorta

The attacks may last for a few minutes or several hours Very often they recur nocturnally and then with extreme punctuality at exactly the same hour They may also be diurnal In some cases as in pheochromocytoma it is possible to reproduce an attack by having the patient immerse the hands in cold water or by mental or physical strain In most cases the attacks come and go without apparent reason The attacks disappear during a febrile episode

Whereas the attacks associated with pheochromocytoma usually occur with increasing frequency severity and duration unless the tumor is removed the attacks reported in this section may disappear at any time and may never recur In several patients with this syndrome who succumbed we searched

very carefully for evidence of the chromaffin tissue or the presence of a chromaffin cell tumor but without success

Hyperadrenalinemia and hyperglycemia have been found during a crisis of this kind (Bernal Kugelmann) but this is not significant since every stimulation of the sympathetic system is accompanied by an increased outpouring of adrenalin like substances into the blood

That these attacks are not due to an increased output of adrenalin alone is shown by the observation that in some of these patients a local vascular spasm appears during the attack In two of our patients marked pallor of the left arm appeared simultaneously with an increase of blood pressure and anginal pain

These local crises may involve the meningeal vessels causing the headache or the cerebral vessels may be affected causing transient paralysis (cerebral crisis) in rare cases local arterial retinal spasm (retinal crisis) was observed causing amaurosis (Pal)

In acute and chronic nephritis and in the malignant phase of hypertension similar general and cerebral vascular crises occur causing increased blood pressure headache vomiting tonic and clonic convulsions coma temporary paralysis and even transient amaurosis Local vascular spasm is responsible

Very rare are depressor crises during which entirely without premonition and without visible cause a considerable fall of blood pressure occurs with weakness general sweating and nausea These attacks last for minutes or hours Their mechanism is unknown Careful observation fails to detect evidence of coronary thrombosis One of our patients with coronary sclerosis who survived two attacks of this type succumbed during a third more than two years after the second

The hypertensive crises are often unrecognized because in the interim examination yields negative results even if a slight aortic insufficiency is found in a young boy or girl the examining physician who does not see the patient in an attack fails to consider the possibility that a quite different syndrome is present when complaints occur Women after the menopause who do not show any abnormality when examined between attacks are considered to be neurotics All gradations between very severe pain and moderate retrosternal pressure are observed Frequently the symptoms are disregarded or considered nervous and sedatives are prescribed

Mechanism The developmental mechanism of this pain is not clear Equally obscure is the problem of why the crisis occurs so often in connection with aortic insufficiency and why only a few patients with this lesion present it Most of the patients originally observed by Pal had an aortic insufficiency and since some of them also suffered from tabetic crises the application of the term *crisis* for a paroxysmal rise of blood pressure seemed indicated

Examination of the blood pressure during an attack makes it clear that the anginal pain develops when the pressure level reaches a certain point Lewis speaks of a vasomotor storm in the splanchnic sympathetic system the cause

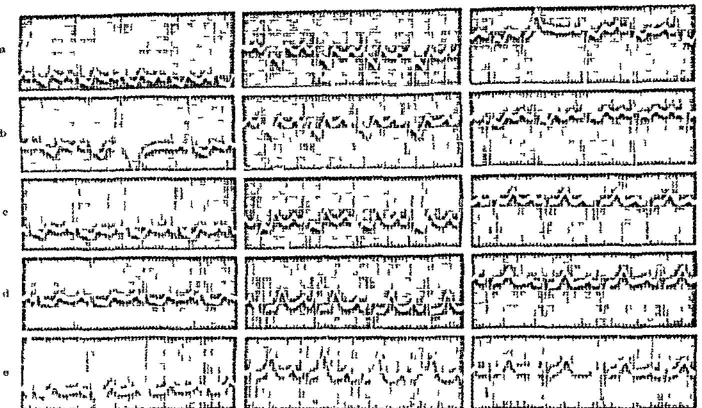


Fig 83 A series of electrocardiograms obtained during a hypertensive crisis with anginal pain

of the abnormal sympathetic vasoconstrictor impulses the reason why they appear and vanish is unknown

If a patient with syphilitic or atherosclerotic coronary stenosis develops this paroxysmal hypertension the occurrence of pain is understandable The sudden rise of blood pressure and the higher heart rate usually associated with it increase the demand for blood if due to coronary disease an adequate supply is not forthcoming pain will result If an electrocardiogram is registered in such a patient during a hypertensive crisis and compared to the electrocardiogram obtained during the anginal pain after physical exertion the two are seen to be exactly the same (Hausner and Scherf) this was noted in 47 cases

Figure 83 was obtained from a 39 year old woman with syphilitic aortitis *narrowing of the orifices of both coronary ostia was found at necropsy* The patient had angina on effort and severe attacks of angina pectoris at rest with good response to nitroglycerin During the attacks appearing at rest the blood pressure rose considerably

The electrocardiogram showed only left axis deviation On exertion marked changes appeared in the T waves The same changes developed during attacks of angina pectoris occurring at rest

The tracing in figure 83a was taken during an attack of severe anginal pain It shows a sinus tachycardia a single ventricular extrasystole in lead III and deeply inverted T waves in each lead The same changes were visible in figure 83b which was registered five minutes later The pain had disappeared in the meantime following the administration of nitroglycerin Figure 83c and figure 83d taken 10 and 15 minutes after figure 83a show gradual improvement The last tracing (figure 83e) obtained 20 minutes after the first one shows almost complete recovery There is still a slight depression of the RS T segment in lead I

These tracings prove the existence of a marked hypoxia of the heart muscle during these attacks persisting even after the pain had disappeared

Patients with an aortic insufficiency may suffer from severe attacks of angina pectoris but the *coronary arteries are found normal at necropsy* (Lewis) *In one* case of this kind among our observations the coronary arteries were normal at necropsy but the electrocardiograms recorded during the attacks were always markedly altered and showed evidence of hypoxia of the heart muscle

One must therefore assume that the pain in these patients probably results from a participation of the coronary arteries with the same narrowing which involves the splanchnic vessels whereby the blood supply to the myocardium becomes insufficient Paroxysmal hypertension also was said to cause narrowing of the coronary arterial tree via the carotid sinus reflexes (Stella) Bilateral denervation of the carotid sinus in two patients with hypertensive crises *however* failed to alter the clinical picture (Scherf 1937)

Therapy Amyl nitrite and nitroglycerin relieve the anginal pain and the headache but the relief is transient within a few minutes the pain recurs The blood pressure may remain high The amount of nitroglycerin which some of these patients take in a twenty four hour period is sometimes staggering As

early as 1905 Pal noted success from only one agent sodium thiocyanate Papaverine al o recommended by this author in our experience is rarely of help

When the attacks recur too often and patients are incapacitated by them paravertebral injections of procaine alcohol are indicated

In three patients with a combined aortic insufficiency and stenosis who suffered from hypertensive crises and severe angina pectoris marked relief was obtained by the administration of thiouracil Four tablets of 0 1 Gm were given daily (Scherf and Terranova 1945) Within 4 to 7 days the patients claimed that they were able to sleep for the first time in weeks the symptoms recurred soon after the thiouracil was replaced by a placebo of the same size taste and appearance The patients felt better again when treatment with thiouracil was reinitiated

ANGINA PECTORIS IN OTHER CONDITIONS

SEVERE ANEMIA

Severe chronic anemias may be associated with serious changes in cardiac function and also with exertional angina pectoris (Herrick and Nuzum) The increased heart rate the greater output the acceleration of blood flow and better oxygen utilization compensate to a large extent for the lack of hemoglobin in advanced anemia This compensation is not ideal for sooner or later the heart suffers

The Heart in Chronic Anemia

Anatomically a fatty degeneration of the myocardium develops particularly in the area around the papillary muscles the area most sensitive to the lack of blood supply This combined with the increased activity of the heart is responsible for cardiac dilatation and hypertrophy Patients with marked dilatation of the heart secondary to anemia are rare nowadays but it still happens that patients with a severe chronic anemia are treated for a long time as cardiacs

Examination of these patients may yield a host of findings The peripheral arteries show a collapsible pulse Duroziez s murmur and a pistol shot sound a capillary pul e may be found Palpation of the precordium di closes cardiac hypermotility Percussion and x ray examination show enlargement of the right and left ventricles with mitralization the result of dilatation of the pulmonary artery and of the left atrium The enlargement does not parallel the degree of anemia and disappears after successful treatment It is absent despite a chronic advanced anemia in bedridden and cachectic patients (Zdansky) The pulsations of the heart are often found accentuated during fluoroscopic examination

A variety of abnormal findings are found on auscultation Tachycardia is usually present Splitting of the first heart sound imitating a presystolic murmur is followed by a loud first sound as in mitral stenosis This presystolic murmur is never drawn out it is very short and probably owes its appearance to the

activity of hyperactive atria It has been pointed out before that the atrial contraction causes a split sound to appear this may be confused with a pre systolic murmur Systolic murmurs over all orifices are the rule and occur mainly because of the increased speed of blood flow Over the apex there may be another loud systolic murmur when the left ventricle undergoes progressive dilatation and a relative mitral regurgitation appears An expansile liver pulse and a positive venous pulse in the neck indicate the presence of a relative tricuspid insufficiency In a few cases high pitched diastolic murmurs are heard at the base of the heart Sometimes they are due to a relative aortic insufficiency sometimes to the speed of blood flow in the veins In this instance the murmurs create a continuous hum with diastolic accentuation the latter is produced by the rapid flow of blood in the large veins close to the heart during diastole

Edema and hepatic enlargement appear in such patients and the mis interpretation of these cases as examples of rheumatic mitral or aortic lesions formerly was a common occurrence

Angina Pectoris in Chronic Anemia

Not rarely these patients complain of anginal pain on exertion However this distress is rarely of sufficient severity for the patient to mention it spon taneously Usually it is necessary to ask direct questions about it In one series of 1560 cases of pernicious anemia angina on effort was recorded in 2 7 per cent (Willius and Griffin) while in another series of 25 cases with a hemoglobin under 50 who were asked directly about angina pectoris on effort the symptom was present in eight (Pickering and Wayne)

In a large percentage of patients with anemia and angina on effort it is not the anemia alone but its combination with coronary sclerosis that causes the pain It is understandable that a coronary sclerosis insufficiently advanced by itself to provoke effort angina may do so when a severe anemia is superimposed Nevertheless instances are known in which an effort angina and severe anemia were associated although necropsy revealed normal coronary arteries

PAROXYSMAL TACHYCARDIA

It has been known for a long time that pain appears in the cardiac region or behind the sternum and radiates to the left arm in patients with paroxysmal tachycardia This pain is not always a minor symptom accompanying paroxysmal tachycardia or paroxysmal fibrillation with a high ventricular rate At times pain is so prominent that the false diagnosis of coronary thrombosis is made This mistake is understandable if the patient relates that he suffered from excruciating retrosternal pain lasting for several hours that radiated to the left shoulder and into the left arm The pain usually lasts as long as the tachycardia The relief afforded by nitroglycerin is temporary Since the increased heart rate is often not felt by the patient during the paroxysmal tachycardia pain alone is mentioned

If the paroxysmal tachycardia recurs pain reappears In one case of paroxysmal atrial fibrillation precipitated by reflexes whenever the patient took a deep breath (Burak and Scherf) pain developed for the duration of the fibrillation which was a few seconds or minutes this patient was treated as an effort angina until the nature of the pain was discovered Quinidine prevented the attacks of fibrillation and the anginal pain did not recur

The ab ence of the usual signs of a coronary occlusion and myocardial infarction following a prolonged attack of pain permits the differential diagnosis There will be no progressive fall of blood pressure and no increase of sedimentation rate It is necessary however to stress that a slight rise of temperature for a few hours hemoptysis and vomiting occur during some attacks of paroxysmal tachycardia

The great reduction of the minute volume during an attack of tachycardia and the decided fall of blood pressure coinciding with the remarkable increase of demand for blood by the heart explains the pain in patients with healthy hearts In patients who already have coronary sclerosis — that is in the majority of those beyond the age of 50 and in those who have a syphilitic stenosis of the coronary ostia — pain is more common during a paroxysmal tachycardia It may be agonizing In one case of syphilitic aortitis which came to necropsy shortly afterward there was narrowing of one and occlusion of the other coronary orifice This patient had to be given injections of morphine whenever a paroxysm of atrial fibrillation appeared with a ventricular rate of 190

Immediately after the onset of a paroxysmal tachycardia evidence of myocardial anoxia may be visible in the electrocardiogram for a short while after the tachycardia subsides abnormal T waves indicate the myocardial damage created by the increased rate (Burak and Scherf) This phenomenon has been named post tachycardia syndrome It was mentioned previously that mere acceleration of the cardiac rate by an injection of atropine in a patient with coronary stenosis may lead to marked alterations in the electrocardiogram

The differential diagnosis between paroxysmal tachycardia and coronary occlusion will be especially difficult if the patient is examined only after the tachycardia has disappeared At that time it may be impossible to ascertain the true cause of the pain Despite the negativity of all findings coronary occlusion with myocardial infarction cannot be completely ruled out

Obviously the prognosis and treatment of this type of angina pectoris is quite different from that of other forms The administration of sufficient doses of quinidine will effect a cure

Hyper and Hypothyroidism

It is not unusual to encounter the typical pain of angina pectoris in hyperthyroidism Usually the pain occurs on exertion or excitement but it is reported to have occurred at rest and during the night The combination of anginal pain

cardiac disease and hyperthyroidism is uncommon before the age of fifty years (Levy and Hamburger) Presumably these patients have coronary sclerosis which alone would not cause angina pectoris When it is associated with the tachycardia and cardiac hypermotility dependent upon hyperthyroidism however the anginal pain appears on effort or excitement

Subtotal thyroidectomy or treatment with thiouracil or radioactive iodine usually affords excellent results

Coronary sclerosis is a common event in myxedema Many patients without previous symptoms develop anginal pain shortly after taking thyroid preparation Sometimes treatment with thyroid is impossible because pain recurs even when very small doses are used

PULMONARY EMBOLISM

Reference was made to the occurrence of angina pectoris in pulmonary embolism in previous sections

Pulmonary embolism may produce many of the symptoms and signs of coronary thrombosis Both may present pain lasting for hours fall of blood pressure and leukocytosis Fever increased sedimentation rate and alteration of the electrocardiogram follow so that the differential diagnosis between the two conditions is fraught with difficulty or may even be impossible Naturally pulmonary embolism rather than coronary thrombosis should receive primary consideration in a bedridden or postoperative patient unless cardiac symptoms suggestive of coronary disease have long been conspicuous To be sure both coronary thrombosis and pulmonary embolism may occur in seemingly healthy individuals without premonitory symptoms An earlier venous thrombosis may have entirely escaped recognition This situation prevails particularly when a traumatic thrombosis develops asymptomatically in a vein of the lower extremities some time after a slight and forgotten trauma

Attention has been previously directed to the fact that the pain associated with pulmonary embolism may last only for a few minutes and it may respond quickly to nitroglycerin The pain may recur repeatedly

CHEST PAINS IN CLIMACTERIC WOMEN

A precordial pain which occasionally radiates into the left arm is a common complaint in patients in the climacterium The symptom is described with great vivacity and is associated with considerable anxiety but it is not related to effort or other ascertainable extrinsic factors

Since objective findings such as hypertension tachycardia and electrocardiographic findings coexist confusion with the angina pectoris of coronary sclerosis occurs This subject will be discussed in a later chapter

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Chapter 17

Cardiac Changes due to Non-penetrating Trauma

THE DEVELOPMENT OF THE AUTOMOBILE increased expansion of industry and the simultaneous improvement of methods of clinical examination have contributed to the increasingly frequent occurrence and discovery of cardiac changes due to blunt trauma Abundant casuistic material that reaches back over a long period has been summarized by Warburg Experimental work on this subject was performed many years ago (Kulbs) but the important results were neglected until interest was revived by new contributions

One speaks of cardiac commotion when a patient dies after an accident involving a blow to the chest in the region of the heart and at necropsy not even a microscopic sign is found In contusion of the heart pathologic changes are visible

Etiology

The accidents responsible for cardiac changes are diverse Stumbling against a sharp object or a fall from a great height partial burial in sand during an excavation steering wheel accidents and chest injury caused by a blow from a rapidly moving object (baseball stone) exemplify some common occurrences It is important to note that cardiac trauma need not necessarily require a pre cordial injury (Bright and Beck) for the heart can rupture when the lower half of the body is exposed to severe pressure in a sandpit When the abdomen and lower extremities are compressed large quantities of blood may be pressed toward the heart and may overfill the chambers the right atrium is commonly ruptured although this may happen to any cardiac chamber Infarction of the posterior wall of the left ventricle has followed fracture of the sternum (contre coup force) Posterior wall lesions as a consequence of blows against the anterior chest wall are frequent in experiments If the elastic chest wall is pushed in by an accident the heart may be pressed between the anterior chest wall and the spinal column

Pathology

Pericardium All three layers of the heart may be injured The most common gross change is the presence of petechiae and hemorrhages in the epicardium Frequently the pericardium is ruptured even when the compressing force was

applied to the abdomen or lower extremities Traumatic pericarditis is not rare and in non penetrating myocardial injuries it appears as a consequence of sub epicardial myocardial damage with necrosis and reactive inflammation Thus it parallels the pericarditis observed after myocardial infarction Hemorrhagic pericardial effusion results from cardiac trauma Secondary calcification occurs

Myocardium The myocardial hemorrhages may extend over a large area Necrosis and softening may appear and perforation of the cardiac wall may follow immediately or after several days In experiments the conus area of the right ventricle is often involved (Scherf and Terranova)

The necrotic areas are often multiple and may be found in all parts of both ventricles A rupture caused by necrosis of the right atrium is most common but any chamber or the interventricular septum may be involved In the injured area edema and disorganization of the muscle bundles with migration of polymorphonuclear leukocytes can be observed within twenty four hours (Moritz and Atkins)

It is important however to emphasize that in a large percentage of acute experiments with a fatal outcome no changes were found at post mortem In experiments on 25 cats anatomic changes were missed in 15 animals despite a fatal ending and the presence of marked electrocardiographic changes Ventricular fibrillation did not occur (Scherf and Terranova) In the hospital wards the same observation may be made A 26 year old man died immediately following a blow over the cardiac area during boxing no abnormality was found at post mortem (Deutsch)

Endocardium Subendocardial petechiae are often seen Rupture of the valves due to direct or indirect trauma has been described frequently the aortic valve is affected more often than the mitral Valvular rupture following slight trauma is prone to occur when the valve is already diseased This is illustrated by the rupture of an aortic cusp and traumatic aortic regurgitation in syphilitic aortitis an accident that is not particularly rare following unusual strain The diastolic murmur appearing in these traumatic aortic insufficiencies is usually musical

Symptoms and Signs

Sudden death may follow blunt trauma of the heart immediately or several weeks after the accident Often patients faint or have severe pain or palpitation extreme weakness may be present Pain may not appear for several hours or even days after the accident however and when late it is often due to the appearance of pericarditis The frequent statement that symptoms must appear instantly or very soon after the accident in order to connect the cardiac damage to the trauma is certainly true in a majority of cases but it is not invariably applicable

In clinical cases and in experiments a marked drop in blood pressure acute dilatation of the heart gallop rhythm and embryocardia (tic tac rhythm) may follow an accident

Since large areas of the heart muscle may become necrotic symptoms and signs may closely resemble those of coronary thrombosis with myocardial infarction Fever fall of blood pressure leukocytosis and an increased sedimentation rate are present There is collapse shock pallor sweating The heart sounds may be faint Mural thrombi and emboli may develop In other cases few symptoms are present In many instances particularly with rest complete recovery takes place Perforation of the septum has been reported Sudden death may occur several weeks after the accident

The myocardial necrosis following blunt trauma may lead to chronic heart disease in the same way that myocardial infarction following coronary occlusion

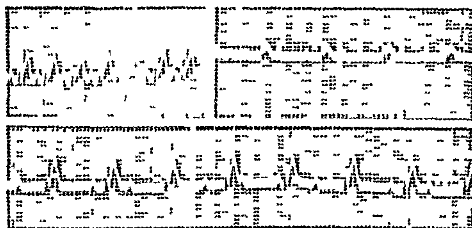


FIG 84 An experiment on a cat A heavy blow was struck on the anterior chest wall Immediately the normal electrocardiogram changes to one with complete A V block and monophasic QRS complexes (high take off) Four minutes later the lowermost tracing was obtained the monophasic electrocardiogram has given place to normal QRS complexes but the heart block persists The first upper (normal) tracing is lead II the other two are lead III (Scherf and Terranova)

lead to chronic heart disease Chronic ventricular aneurysm may appear An existing heart disease may be aggravated

It is important to re emphasize that serious damage and even rupture of the heart sometimes follows blunt trauma in the absence of a visible external injury (Hamilton Kellert)

Arrhythmias Variform arrhythmias are very common They are often observed clinically and experimentally The simplest and most common type consists of extrasystoles which may arise in any part of the heart Sinoatrial block and atrioventricular rhythm also occur Atrial and ventricular fibrillation paroxysmal atrial and ventricular tachycardia and any type of partial as well as complete heart block have been observed (figure 84) These changes stem partly from hemorrhages and necrosis but temporary mechanical irritation of the muscle fibers also plays a great part

Electrocardiogram Electrocardiographic changes are very common an electrocardiogram should be taken in every accident in which cardiac involvement might be present

In addition to arrhythmias the electrocardiogram may show changes due to pericardial and to myocardial damage The alterations of the QRS complex and T waves resemble those of other myocardial lesions Even a high take off similar to the one of coronary thrombosis has been observed This was ascribed to coronary spasm induced by the mechanical irritation of the coronary arteries (Schlomka) but the high and low take off appears with the first beat after the trauma much too soon to be explained by coronary artery spasm Such changes are better explained by a direct mechanical derangement (depolarization) of the superficial muscle layers resulting from the blunt trauma (Scherf and Terranova) Similar transient changes are encountered after mechanical irritation of the exposed heart They disappear within minutes (Boyd and Scherf) Since mechanical irritation of the coronary vessels as in the case of other arteries may be followed by local vasoconstriction (Drury and Smith) a local coronary spasm is not impossible in some cases This can only cause secondary changes appearing 40 to 60 seconds following the trauma

The physician should always think of the possibility of a laceration of the heart particularly of the right atrium in direct compression of the abdomen Lives are saved by the correct diagnosis and successful suture of the atrium (Desforges et al)

CORONARY THROMBOSIS AND TRAUMA

A question of great interest and importance is the possible appearance of coronary thrombosis following non penetrating trauma Clinical cases in which coronary thrombosis developed after an accident have been reported in increasing numbers in recent years Possibly such accidents result from rupture of a giant capillary in a sclerotic coronary artery or a rupture of an atheromatous abscess Exact data to prove this occurrence do not exist Usually a relation is assumed if the symptoms and signs of a coronary occlusion appear immediately after or shortly after a trauma but as mentioned earlier symptoms and signs may not develop for hours Since trauma causes myocardial necrosis at times over a large area without involvement of the coronary arteries it is difficult to differentiate between myocardial infarction due to coronary occlusion and myocardial necrosis resulting from contusion of the heart As pointed out before most of the signs may be identical in both instances

The history has paramount importance in establishing the connection between an accident and the cardiac involvement While the appearance of a coronary occlusion following precordial trauma and compression of the chest wall in the antero posterior direction in cases with coronary sclerosis is very probable although not established beyond all doubt the occurrence of a coronary occlusion from abdominal trauma or after lifting heavy objects is dubious although not impossible

On the other hand a case has been observed in which a helper on a truck suffering an attack signalled the driver to stop and then collapsed on the floor of the truck The driver swung out of traffic but in so doing dislodged part of the load which fell upon the already stricken helper

X RAY THERAPY ELECTRICAL ACCIDENTS

Very serious myocardial damage is frequently observed following deep x ray therapy (or radium implantation) in the cardiac area We saw repeated evidence of cardiac failure with tachycardia gallop rhythm and pulmonary congestion develop following deep x ray therapy for Hodgkin s disease or mediastinal malignancy

Pericardial irritation due to x ray irradiation has been mentioned

A voluminous literature exists on experimental and clinical observations of atrial and ventricular fibrillation in connection with electrical accidents

Therapy

Treatment consists of bed rest symptomatic measures and in the case of cardiac rupture surgery Since many cases of serious myocardial lesions are reported to follow comparatively minor trauma and since persistent searching more and more frequently turns up evidence of traumatic cardiac lesions it seems advisable to examine electrocardiographically and by x ray every patient involved in such an accident Bed rest should be continued until cardiac involvement can be definitely eliminated Early signs of cardiac tamponade should be looked for

While recoveries were rare in cases reported by the original investigators their number increases with careful observation Originally only very serious cases with cardiac rupture traumatic aneurysm and the like were reported but at present milder injury is often described Chronic heart disease with long invalidism does occur

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Chapter 18

The Heart in Endocrine Disorders

Hyperthyroidism

Hyperthyroidism can disturb cardiac action very profoundly but the alterations are not invariable nor when present do they always develop with the same speed and to the same degree Sometimes patients manifest all features of hyperthyroidism but display no evidence of cardiac involvement save for an insignificant tachycardia Even this may be absent On the other hand patients with an apparently mild hyperthyroidism may develop cardiac dilatation and evidence of congestive heart failure within a short time

Incidence

The affection is more common in women than in men Its incidence varies considerably in different localities being most frequent in the Great Lakes basin of the United States and in the Alpine regions of Europe It occurs at all ages we have encountered it in children of five years and in people beyond seventy

Pathology Pathophysiology

At necropsy about 50 per cent of patients dying from hyperthyroidism show cardiac hypertrophy and dilatation These changes may be absent even in very toxic cases and they are uncommon in elderly cachectic patients who have lost much weight There is no parallelism between cardiac size and degree of hyperthyroidism

The mechanism of cardiac enlargement is obscure In some cases it may be explained by the presence of a coronary atherosclerosis a complicating hypertension or atrial fibrillation that was untreated or that failed to respond to treatment It occurs however without these complications

The increased rate hardly contributes to the changes but the increased motility which seems to result from a direct action of thyroxin on the myocardial fibers and the increased load on the heart may tire the muscle and lead to dilatation Histologic examination fails to reveal characteristic or consistent lesions physico chemical changes that are not revealed by histologic examination may be responsible Contrary to the frequently expressed opinion it is noteworthy that cardiac enlargement and failure may be found in young people or even adolescents with pure hyperthyroidism without other demonstrable compli

cations Naturally a patient with a slight rheumatic lesion coronary sclerosis or syphilitic heart disease tends to develop decompensation earlier if hyper thyroidism coexists In 176 fatal cases congestive heart failure existed 27 times in a majority of these complications such as coronary sclerosis rheumatic heart disease and syphilis were found (Kepler and Barnes)

Symptoms

The symptoms of thyroid hyperfunction will not be discussed here The dyspnea is partly due to increased metabolism and rarely to pulmonary congestion Sighing respiration is often responsible Palpitation is a very common complaint and is evoked by the marked cardiac hypermotility or paroxysmal fibrillation Attacks of paroxysmal atrial fibrillation are often observed Angina pectoris occurs as was mentioned before, it is found only in elderly patients who in addition to hyperthyroidism also suffer from coronary disease

Signs

The description of the signs will be limited to those of the cardiovascular system

Palpation Extremely powerful quick pulsations over the precordium may shake the whole thorax and suggest a much larger heart than actually exists These pulsations are most easily palpable near the conus of the right ventricle

While an increased pulse rate is usually present it is not rare for a normal sinus rate or even bradycardia to occur Often the pulse has all the characteristics of a water hammer pulse as in aortic insufficiency

Blood Pressure The pulse pressure occasionally shows a marked increase since the systolic pressure may rise to 180 mm Hg or more and the diastolic pressure often drops to below 50 mm Hg This thyrotoxic systolic hypertension is caused by the hypermotility of the heart

Percussion and X ray Examination Percussion reveals a normal or a mitralized heart dilated to the right and left The incidence of dilatation is higher in patients with old and advanced hyperthyroidism and with other complications *Therefore the figures vary with the clinical material* It is least common in areas where the diagnosis is made early and therapy is employed quickly

Fluoroscopy reveals marked hypermotility of the heart and pulsus celer of the aorta The pulmonary artery is dilated in one third of the patients This is probably not due to constitutional factors as has been stated nor to persistence of juvenile conditions but rather to a dynamic dilatation caused by the hyper motility of the right ventricle The aorta may also show dynamic dilatation In hyperthyroidism with heart failure the lung fields are clear as the right ventricle dilates and fails from the start

Auscultation Often the heart sounds are abnormally loud A short pre systolic click caused by the contraction of the hyperactive atrium may cause

confusion with mitral stenosis Systolic murmurs are very common over the pulmonary artery and aorta and are due to the increased speed of blood flow Extracardiac venous murmurs like those present in anemia are frequently heard If they appear in diastole and the peripheral pulse is of the Corrigan type the erroneous diagnosis of aortic insufficiency may be made In a patient with hyperthyroidism seen by one of us a large adenomatous nodule that compressed the left subclavian artery produced a double Duroziez murmur at the left sternal border imitating an aortic insufficiency The increased speed of the circulation causes a diastolic venous hum over the large veins A pericardial friction rub is not rare over the prominent conus of the pulmonary artery It results from the friction between normal epicardium and normal pericardium and should not be mistaken for a real pericarditis Relative aortic insufficiency has been described but it is possible that a diastolic murmur in these cases was evoked by one of the mechanisms just mentioned

Electrocardiogram The electrocardiogram does not help in the diagnosis It is normal or shows only sinus tachycardia Abnormalities of the T waves are rare Depression of the RS T segments is noted occasionally

Laboratory Tests The serum protein bound iodine permits an estimation of the level of the circulating thyroid hormone Also useful is the determination of the level of radioactive iodine uptake with tracer doses of I^{131}

Complications

Hepatic enlargement and edema appear late Atrial fibrillation is a common complication but its appearance in hyperthyroidism has not as yet been fully explained It often occurs in short paroxysmal attacks but soon becomes constant unless abolished by successful treatment of the hyperthyroidism Due to the high sympathetic tonus the ventricular rate is rapid and characteristically the rate does not slow quickly under treatment with digitalis Extrasystoles are not very common an astonishing fact in view of the great frequency of fibrillation

Differential Diagnosis

The diagnosis is very easy in typical cases but may be difficult in others In mild cases the presence of low fever cardiac symptoms and signs may lead to the diagnosis of rheumatic heart disease or subacute bacterial endocarditis In very advanced cases the cardiac enlargement and right ventricular failure suggest the diagnosis of a decompensated mitral lesion In the latter condition the left atrium usually is markedly dilated whereas it is normal or only slightly enlarged in hyperthyroidism the differentiation is sometimes difficult The situation is rendered more confusing since in cardiac lesions an increased basal metabolic rate of 50 per cent or more is not rare and other signs of hyperthyroidism such as wasting excitability and tremor may also appear Finally it may be difficult to distinguish between mild hyperthyroidism and cardiac neurosis

Physicians must always be on the alert not to overlook masked hyperthyroidism appearing as atrial fibrillation of the chronic or paroxysmal type heart failure and the like

In many cases the evidence of cardiac involvement is so much in the foreground that the attending physician overlooks the hyperthyroidism which is the etiologic factor and treats the patient symptomatically only for his cardiac complaints With more careful examination and with consideration of the hyperactivity of the patient his nervousness his inclination to perspire easily and so forth the correct diagnosis will be made

Treatment

As soon as hyperthyroidism is recognized specific therapy should be started This may be accomplished with the methods of bloodless surgery that became available in recent years Propylthiouracil is given daily (400 mg) in 100 mg doses with continuous supervision of the white blood cell count As soon as improvement is noted the dose is reduced to 50—100 mg daily Tapazole (mercapto imidazole) may be given initially in doses of 40 mg daily and later 5—20 mg daily Skin irritation and fall of the leukocyte count occasionally preclude continuation of the treatment

Within three months after the discontinuance of this therapy a relapse may be expected in 23 per cent of the patients In another 20 per cent relapses occur later A lasting effect is accomplished in only about 50 per cent of the cases with one series of treatments

Therapy with radioiodine has a much larger percentage of permanent success It is the method of choice in the elderly patient

Surgery is indicated for hyperthyroidism alone if for certain reasons the patient cannot undergo medical therapy

Signs of hyperthyroidism are not rare in the climacterium and they complicate the picture (see below)

HYPOTHYROIDISM

Just as the cardiac alterations may be surprisingly slight despite marked hyperfunction of the thyroid there are instances of marked hypothyroidism with a basal metabolism more than 30 per cent below normal with normal circulatory findings It is unknown why cardiac abnormalities appear early in one case and are absent in another The infrequency of cardiac abnormalities in a fair percentage of cases was the chief reason the existence of a myxedema heart was often denied in the past

Symptoms

In an uncomplicated case of myxedema with marked cardiac involvement there are no typical cardiac complaints The lassitude and general weakness are not characteristic and it is uncommon for the patient to seek advice for dyspnea

or edema However a complicating angina pectoris due to coronary sclerosis often causes the patient to ask for medical assistance

Signs

The heart may be enlarged to the right and left Marked flatness is often percussed over the precordium On fluoroscopy the pulsations of the cardiac borders are sluggish and in some patients the borders scarcely move The heart sounds are muffled and distant Rough systolic murmurs over the aortic or mitral valve when present are due to atherosclerotic changes The blood pressure is normal or moderately elevated Bilateral or right sided hydrothorax is common

In a typical uncomplicated case the electrocardiogram shows low voltage of all waves in each lead the P and T waves may disappear completely and the QRS complexes are often only a few millimeters in height

Differential Diagnosis

Few diseases are so often overlooked as myxedema Errors occur even in fully developed forms with typical alterations in the skin puffiness of the face the deep harsh voice sensitivity to cold slow motor and psychic reactions in which the diagnosis should be apparent at a mere glance Most often some intrinsic cardiac disease is diagnosed because of the finding of cardiac enlargement edema hepatic enlargement and electrocardiographic abnormalities Very often these patients have been subjected to long courses of digitalis which afforded no relief The albuminuria and facial edema may lead to a diagnosis of nephritis The accompanying anemia leads to liver and iron therapy and often the headache and constipation are treated symptomatically without the basic malady being recognized

Pathology

Formerly the cardiac alterations were ascribed to myxedematous swelling of the myocardial fibers Histologic examination often shows fibrosis or degeneration of these fibers but in many cases this is due to the coexisting coronary sclerosis in any event these changes are not pathognomonic In recent years an increasing number of observations indicate that a pericardial effusion is present in a large percentage of cases Pericardial effusions are observed after thyroidectomy in sheep goats and rabbits The diagnosis of a pericardial effusion was confirmed by paracentesis in eleven patients seen by us in recent years The flatness over the precordium the sluggish contractions of the heart on fluoroscopy and the low voltage in the electrocardiogram are easily explained by a pericardial effusion To be sure sluggish contractions also occur in myocardial lesions but rarely to an equal degree unless the heart muscle has suffered unusually severe damage Moreover a pericardial effusion more readily explains the rapid restoration of normal cardiac diameters following the administration

of thyroid substance In a myocardial disease it is rare for one to observe a markedly enlarged heart return to normal size with equal speed and to a similar extent

Pericardial effusions with a very high content of cholesterol in the pericardial fluid occur in the absence of myxedema and with a normal blood cholesterol level their origin is still unexplained

To what extent the cardiac enlargement must be attributed to a pericardial effusion in a given case of myxedema is often difficult to ascertain

Complications

The most common and most important complication of myxedema is coronary sclerosis This is a regular event in chronic cases and is presumably connected with the hypercholesterolemia Some electrocardiographic findings in myxedema such as abnormal T waves and a prolonged P P interval as well as the cardiac enlargement and fibrosis on histologic examination are due to coronary sclerosis and not to myxedema Owing to this complication patients with myxedema often develop angina pectoris Coma as well as maniacal excitement occur (Summers)

Treatment

Great care is necessary in therapy with thyroid substance or thyroxin Often the doses used are excessive and much harm can be done One tablet of 0 01 Gm thyroid given daily often suffices sometimes smaller doses must be *given* The patient should be watched continuously *since the cardiac* situation may become worse as the metabolism reverses to normal although the myxedema is improved the increased heart rate and increased oxygen consumption of the heart may be injurious in the presence of coronary sclerosis Frequently it will be found more advantageous to allow the patient to retain a low metabolic rate than to treat the myxedema and initiate severe attacks of angina pectoris Occasionally we have seen angina pectoris on effort disappear following the administration of thyroid extract

Like hyperthyroidism myxedema may develop during the endocrine imbalance of the climacterium

OVARIAN HYPOFUNCTION AND THE FEMALE CLIMACTERIUM

Incidence

Few women are entirely free from complaints during the climacterium An inquiry among 1000 women of all ages revealed that only 15 8 per cent went through the critical age without annoying symptoms (Council) In another series of 1000 cases symptoms were found in 85 per cent (Hawkinson) Many suffer from a host of disturbances and not a few are even incapacitated (*10 3 per* cent)

Among the diversified symptoms cardiovascular complaints are very common In 1000 women tachycardia palpitation and dyspnea occurred in 70 per cent (Hawkinson) Another observer found the same symptoms in 68 8 per cent of his patients (Werner) About 22 per cent of all women coming to a cardiologist for advice have complaints referable to disturbances of the activity of the ovaries Substitution therapy affords complete relief

Symptoms

General Emotional instability irritability and exhaustion are the chief symptoms in many cases and mental disturbances similar to those of involutional melancholia may occur In other patients gastrointestinal or cardiac complaints are in the foreground Still others have rheumatic pains complaints due to osteoporosis sleeplessness and dizziness

Hot Flushes The outstanding complaint in about 60—85 per cent of the patients is the flush Sometimes after a slight aura consisting of nausea the patient feels a wave of heat ascend to the face and arms immediately followed by a chill and cold sweat The developmental mechanism of this complaint which is not found in any other condition is not as yet fully explained

Dyspnea Many women suffer from the three classical complaints of cardiac patients dyspnea palpitation and cardiac pain The dyspnea may be very pronounced Detailed questioning soon reveals that it consists of a peculiar inability to get the breath through the sighing respiration discussed in the first chapter Only after obtaining information from the doctor does the patient recognize the sighing respiration as the reason for her breathlessness A few explanatory words will go very far to relieve the patient from the extreme apprehension connected with this sensation

Palpitation The palpitation of these patients is independent of exertion and excitement and lacks the characteristic features of the palpitation of a paroxysmal tachycardia that is of sudden onset and ending Often it occurs together with the hot flushes the association is particularly common at night

Pain Pain in the cardiac area is the third important symptom to make the patient heart conscious and apprehensive The pain appears over the precordium (not behind the sternum) and sometimes spreads to the left shoulder and left arm It is not provoked by exertion or excitement and it may last for hours In a majority of these patients examination reveals an area of exquisite tenderness at the fourth (more rarely fifth) rib to the left of the sternum at the costochondral junction (Scherf and Klotz) Rarely the tenderness is found at the fourth and fifth rib of the same patient Infiltration of this small spot with procain affords immediate relief It is possible that local arthritic (osteochondritic) or arthralgic changes account for this complaint as is the case in other menopausal arthralgias According to Staehelin inflammatory processes of the cartilages of the ribs are not rare The connection with ovarian dysfunction is proved by the disappearance of the pain in a few weeks following the administra

tion of sufficient doses of estrogen These complaints are easily separated from those in Tietze s syndrome with marked swellings of the cartilages

Other Symptoms In addition patients often complain about paraesthesias such as numbness and tingling in the fingers and toes as well as headaches Vertigo is common Insomnia abnormal worrying weeping edema of the face foot and calf are not rare

Signs

Sometimes examination reveals nothing abnormal save the sighing respiration and the circumscribed tenderness over the fourth rib In other patients however objective findings are present

The heart may show a marked hypermotility even when there is no evidence of hyperthyroidism A sinus tachycardia up to 120 may be present There may be a moderate hypertension and the electrocardiogram occasionally shows changes of the RS T segments and abnormal T waves (Scherf) Estrogens disappear from the urine and the amount of gonadotropic hormone increases

Hypertension The question of a climacteric hypertension has vexed workers and the subject is controversial Some authorities find the blood pressure elevated in as many as 50 per cent of the cases while others regard any increases of the blood pressure during the climacterium only as a coincidental and unrelated finding (Pal) Since most of the women concerned are at an age in which the blood pressure is often elevated a decision is difficult On the other hand patients with the syndrome described and hypertension so often have the blood pressure fall to normal levels during treatment with estrogen that a relation cannot be denied Such patients are seen more often in private practice than in the hospital In many cases hypertension disappears within a few weeks following the administration of estrogens while in others prolonged treatment is necessary Marked fluctuation of the blood pressure is common In this and other types of hypertension if the blood pressure stays at a high level for some time it becomes fixed and estrogen treatment will not lower it but will only alleviate some symptoms

Taylor et al examined 179 castrated women and 21 with a natural menopause and found that within a three year period hypertension occurred in the same incidence as in the general population This merely emphasizes a fact known for a long time namely that the lack of the estrogenic hormone per se does not cause hypertension The imbalance of the endocrine glands (hypophysis adrenals) may cause hypertension years afterward This occurs sometimes more than three years after panhysterectomy

Women in whom panhysterectomy was done 5—10 years previously occasionally suffer from fixed hypertension Due to the absence of symptoms these patients reach the physician too late In our opinion the blood pressure of women after panhysterectomy should be checked at regular short interval for at least 10 years after the operation and estrogenic treatment should be administered as soon as it is indicated Borgstroem reports excellent results of treatment with estrogenic and androgenic hormones in essential hyperten ion

Electrocardiogram The electrocardiographic changes do not depend upon the presence of a hypertension and are independent from an existing hyperthyroidism They disappear promptly after the administration of estrogens in sufficient doses

Figure 85a shows the electrocardiogram of a 54 year old woman who developed flushes paraesthesias palpitation and precordial pain The heart showed a marked hypermotility and the blood pressure was 160/90 mm Hg The electro

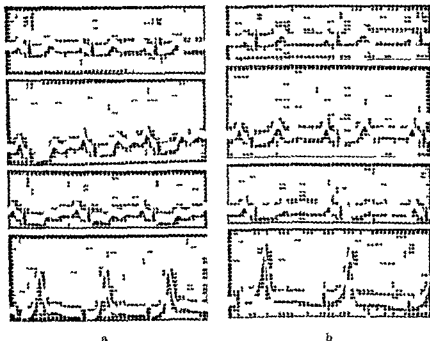


FIG 85 A 54 year old woman presenting the climacteric syndrome before (a) and after (b) treatment

cardiogram shows a depression of the RS T segments in each standard lead and in CR4 The heart rate is 94 beats per minute

Following the daily administration of 0 5 mg of diethylstilbestrol for four weeks the electrocardiogram of figure 85b was obtained It shows a heart rate of 70 and normal RS T segments The symptoms disappeared and the blood pressure was 138/85

Atherosclerosis The more common occurrence of atherosclerosis in man as compared to woman has been known for many years Lately clinical and experimental observations speak for a protective action of the estrogenic hormone Women following natural or artificial menopause show atherosclerosis more frequently than women who are normally menstruating Experimental results were mentioned in a previous chapter Oliver and Boyd found that small doses of ethinyl estradiol depressed plasma ester cholesterol in men This compound has an antiatherogenic action

Pathogenesis

Vascular Effect It is still impossible to explain how these changes originate Since female sex hormones seem to be vasodilators since paraesthesias and acrocyanosis appear in these patients and since vasodilators help the changes may rest on a vascular basis

Electrolytes It is also known that sex hormones like other steroids have a great influence on the electrolyte metabolism particularly on sodium and calcium metabolism It is thus possible that the electrocardiographic alterations can be explained by tissue changes induced by an abnormal electrolyte balance The arthralgias as well as other manifestations of the climacterium may also be caused by one or both of these mechanisms

Hormonal It seems generally agreed that diminution or cessation of normal ovarian function leads to overactivity of the anterior hypophysis the dissenting opinions are in the minority The response of the pituitary leads to oversecretion of the thyrotropic and adrenotropic hormone and results in abnormal function of these glands The resulting clinical pattern as well as the complaints of the patient depend upon the balance of the endocrine system and the status of the patient s autonomic nervous system There is suggestive evidence of a hyper sensitivity of the sympathetic nervous system in the menopause

Estrogen deficiency alone is not responsible Panhysterectomy in young women is often unassociated with symptoms Sometimes manifestations occur years later Flushes and other symptoms may be present despite remarkably high amounts of estrogens in the urine Estrogens may be found in women of 70 and more On the other hand flushes and other complaints may appear while menstruation is normal Probably the imbalance of the endocrine system causes the syndrome in a way which is still obscure

Diagnosis

Naturally in women with complaints referable to the heart with edema hypertension and electrocardiographic changes organic heart disease is often diagnosed We have observed such women put to bed for several weeks with a diagnosis of coronary occlusion or myocarditis sometimes digitalis is used because it is thought the patient is decompensated

It is necessary to emphasize that the climacterium and the menopause are not synonymous The characteristic flushes as well as other symptoms and signs mentioned previously may appear years before or after the cessation of menses They are not very unusual in girls 16 to 18 years of age if they have hypo ovarianism and they may be noted for the first time in women at the age of 70

If the physician attributes the complaints to a change of life the young patient may indignantly explain that she is still menstruating normally while the elderly one may find the diagnosis ridiculous because she has not menstruated for years

Organic Heart Disease and the Climacterium

It has long been the experience of clinicians that patients with an old fully compensated rheumatic valvular lesion or hypertension may develop decompensation during the climacterium In view of the alteration found in women with healthy hearts during the climacterium the increase of blood pressure and the tachycardia these events are understandable All these patients deserve careful supervision during this period and estrogens should be administered in sufficient dosage If this is done full compensation may be preserved for many years without other measures

Myoma (Fibroid) Heart

For many years the status of the heart in patients with uterine fibroids so called myoma heart was widely discussed in medical circles Time and time again changes were described and then challenged Some attributed the changes to the anemia to toxic or mechanical factors acting on the circulation while others found evidence of cardiac damage in the absence of these complications The diagnosis of myoma heart as a clinical entity was rightly abandoned In all probability most of the changes found in these patients are due to the mechanisms mentioned above since such tumors often develop or produce symptoms at the menopause or later

Treatment

The administration of estrogens usually affords striking improvement of the cardiac symptoms in a short time and causes the irritability of the patient to disappear The effect on the tachycardia hypermotility as well as on the hyperthyroidism and hypertension of these patients is equally satisfactory The help given to this group of patients is great

Oral medication usually will suffice Treatment must be persistent often for months occasionally for years In some patients a full therapeutic effect is attained with small amounts orally administered in others particularly those with marked hypertension parenteral therapy with large doses is necessary Inadequate dosage is a very common cause for therapeutic failures If treatment with estrogens becomes necessary in women who are still menstruating the preparations are best given for the first two weeks after the menstrual flow At a later period in the menstrual cycle estrogens may delay the onset of menstruation overdosage may prevent its appearance Often estrogen plus androgen mixtures are useful

The beneficial effect of estrogenic therapy has done a great deal to cause abandonment of the conception of a climacteric neurosis as the cause of complaints

The administration of nonhormonal estrogenic substances such as diethylstilbestrol has the advantage of inexpensiveness While the action is satisfactory toxic effects occur

Before estrogens were available in large effective doses x ray radiation of the hypophysis was recommended in these patients this method has value in selected cases Sedatives like phenobarbital and chloral hydrate support estrogenic therapy in the early stages

Peripheral vasodilation has been reported following the administration of estrogenic substances and this led to their use in peripheral vascular diseases and angina pectoris Available evidence is still insufficient to establish their value in these patients However the effect of estrogens on the development of atherosclerosis is apparently established

Male Climacterium

In males cessation of gonadal function does not occur as suddenly as in females therefore the endocrine and autonomic nervous system have more time for adaptation to the new situation Many authorities deny the existence of climacteric symptoms in men We are convinced they do occur even to the extent of typical flushes with chills and sweating They are however rare Paraesthesias irritability sleeplessness and chest pain of the anginal type are observed The 17 ketosteroids in the urine tend to be low In these patients improvement has been observed after the administration of androgens (McGavack) Usually 25 mg per intramuscular injection twice weekly and a total of 10 or 12 injections are advised Normalization of the electrocardiogram of such patients follows The altered electrocardiogram of female patients with the syndrome discussed above may revert to normal also when male hormones or desoxycorticosterone is given (Scherf and McGavack) For the differentiation from neuroses Heller recommends a therapeutic test with androgens These bring about a rapid improvement in patients with the male climacterium

OTHER ENDOCRINE DISEASES

In this section brief reference will be made to cardiac and circulatory disorders in other endocrine disturbances Some of these changes have great theoretical interest but they are of minor clinical importance because other *manifestations* of the endocrine disorder are *in the foreground* Some of the lesions were or will be discussed in other chapters

In patients with an eosinophilic adenoma of the pituitary and acromegaly enlargement of the heart and cardiac failure is reported

In patients with basophilic adenoma of the pituitary and adrenal cortical tumor (Cushing s syndrome) hypertension and atherosclerosis are common

Diseases of the hypophysis or hypothalamus occasionally cause orthostatic hypotension

The syndrome caused by benign pheochromocytoma of the adrenals is discussed in the section on hypertension In Addison s disease an astonishing reduction of cardiac size is observed during the crisis due to a diminished quantity

of circulating blood (McGavack) Marked changes are found in the electrocardiogram as a consequence of the disturbances of electrolyte metabolism In hyperaldosteronism hypertension is the rule

Administration of excessive amounts of desoxycorticosterone may lead to cardiac enlargement and to evidence of pulmonary congestion (Paab)

In hyper and hypoparathyroidism alterations of a characteristic nature appear in the electrocardiogram and concern the length of the RS T segments caused by the altered calcium metabolism

Hyperfunction of the Langerhans islands due to adenoma or malignant tumor may lead to attacks of hypoglycemia which closely imitate attacks of coronary occlusion with anginal pain (Ernstene and Altschule) It has been pointed out that hyperadrenalemia as the consequence of hyperinsulinism may be responsible for this Hypofunction of the islands of Langerhans with hyperglycemia does not cause cardiac changes

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Chapter 19

Cor Pulmonale

COR PULMONALE IS NOT A DISEASE SUI GENERIS but a symptom complex always encountered when the right ventricle is subjected to increased demands because of hypertension in the lesser circuit The latter is caused by pulmonary vascular disease or deformities of the chest Increased pressure due to mitral valvular lesions or left ventricular failure is not included in this chapter Chronic emphysema with chronic bronchitis is the most common cause

A distinction is made between acute subacute and chronic cor pulmonale The acute form has been discussed with the syndrome of pulmonary embolism The subacute form is seen in status asthmaticus in chronic pulmonary embolization and in pulmonary carcinomatosis (lymphogenous or hematogenous spread) The chronic form is seen in a variety of lung diseases and abnormalities of the thoracic cage

Cor pulmonale is found to be a common condition if a careful search is made for it Clinical statistics showing its incidence are unreliable because the diagnosis is difficult The pulmonary disease is often overlooked and the patient is treated as a primary cardiac

Incidence and Pathology

Cor pulmonale occurs in conjunction with three groups of pathologic conditions

(1) Cor pulmonale may be present in subacute or chronic diseases of the pulmonary parenchyma Chronic bronchial asthma or chronic bronchitis emphysema and pulmonary fibrosis due to pulmonary tuberculosis pneumoconiosis and even bronchiectasis with recurrent pneumonias and infection often present the picture of cor pulmonale It may be seen in Boeck s sarcoid in sickling disease and in schistosomiasis Arvidson et al described four patients with pulmonary hypertension caused by malformation and stenosis of the branches of the pulmonary arteries

In addition to the well known forms of pulmonary fibrosis and pneumoconiosis the idiopathic interstitial acute diffuse fibrosis (Hamman Rich disease) should be mentioned Here extreme dyspnea and cyanosis with marked hyper

trophy of the right ventricle develop quickly within a few weeks There is slight fever and a moderate leukocytosis Hemoptysis and cough appear Postmortem examination reveals an inflammatory nonspecific process of unknown origin There is necrosis of alveolar epithelium with fibrin in the alveolar wall A virus infection has been suspected as an etiologic factor

(2) The picture of cor pulmonale develops in the rare type of essential (idiopathic primary) pulmonary hypertension Syncope occurs and sudden death is common Essential pulmonary hypertension for the most part is a syndrome encountered in women between the age of 20 and 30 years They complain of dyspnea pain on exertion palpitation fainting on effort and cyanosis There is evidence of marked right ventricular hypertrophy and dilatation the second pulmonic sound is very loud and there is no intrinsic pulmonary disease It is possible that in some of these patients minute pulmonary emboli that go unrecognized over years are responsible (Owen et al Barnard) Patients with essential pulmonary hypertension often die suddenly

(3) The same syndrome develops when respiration is disturbed by chest deformities Kyphosis does not lead to cor pulmonale On the other hand scoliosis does because of the emphysema and local infections leading to hypoxia In patients with a funnel chest the heart usually escapes compression by shifting to the left half of the chest and surgical intervention is rarely needed Right bundle branch block not rarely appears in the electrocardiogram Chronic bronchial or tracheal stenosis — the latter for example resulting from a nodular goiter — may also cause right ventricular hypertrophy the mechanical goiter heart In these patients the abnormal respiration alters the negative pressure within the chest and thus disturbs the chief factor aiding the return of blood to the heart Atelectasis and collateral emphysema appear and increase the pressure in the lesser circuit Disturbances of respiration also lead to an abnormal blood flow within the lung from the right ventricle to the left atrium

In emphysema it is not the loss of elasticity of the tissue and the closure of capillaries that leads to hypertension in the lesser circuit and to cor pulmonale Rather in all probability it is the narrowing of the vessels due to local foci of anoxia (as pointed out below) this explains why in many patients with emphysema the pulmonary pressure was found with catheterization to be normal Therefore all infections which lead to the secretion of mucus and occlude small air passages must be treated early with antibiotics Such infections need not cause fever (Flint) The precipitating cause of heart failure was an acute respiratory infection in 74 out of 76 patients with cor pulmonale Penicillin is given by injection and by aerosols in addition terpin hydrate aminophyllin potassium Vaponephrine (5—8 drops three times a day) and Isuprel (1 200 aerosol inhalation) are used The great fatigue is often caused by a relatively too small cardiac output A supporting lower abdominal belt is used and better movement of the diaphragm is accomplished by pneumoperitoneum In those patients who develop polycythemia phlebotomy is performed

Physiology

Normal pulmonary arterial systolic blood pressure varies between 15 and 25 mm Hg and the diastolic pressure is between 6 and 10 mm Hg The blood pressure in the lesser circuit does not rise even when more than 50 per cent of the pulmonary arteries are ligated

Anoxia causes an increase of blood pressure in the systemic as well as in the lesser circuit This is explained in part by an increase of the stroke volume (Cournand Wiggers et al) but an increase of peripheral resistance plays an important role This is mediated according to von Euler and Liljestrand by the oxygen content of the blood acting directly on the arterioles without participation of the autonomic nerves Others assume that anoxia of the carotid sinus and aortic body leads to vasoconstriction in the lesser circuit via axon reflexes (Aviado et al) Little is known about the effect of carbon dioxide retention on pulmonary arterial blood pressure

Since pulmonary infections do cause local anoxia this can result in widespread vascular spasm and an increase of pressure provided it involves large areas of the lung

Even larger pulmonary arteries become narrowed according to von Euler and Liljestrand Thus a local chemical self regulation exists in the lesser circuit which may explain many of the clinical data that defied explanation up to the present The sudden appearance of cardiac failure in a patient with chronic emphysema may be due not only to hypoventilation but also to a sudden rise of pressure because bronchitis with infection causes the formation of mucous bronchiolar obstruction and local hypoxia Actually the old explanation of the cor pulmonale in emphysema was never satisfactory in its assumption of wide spread destruction of capillaries and consequent diminution of the vascular bed Against this was the experience just mentioned that too much of the vascular bed must be destroyed before pressure in the lesser circuit rises Cor pulmonale does not appear if the surgeon removes the right or left lung If we assume that a patient with chronic emphysema develops local anoxia because of bronchitis or local hypoventilation such experiences are now explainable This acute rise of pressure in the lesser circuit causes not only right heart failure but also death

Chronic anoxia and oxygen undersaturation of the arterial blood in the systemic circulation may lead particularly in emphysema with bronchitis or pneumonia to a syndrome of lassitude weakness stupor and coma caused by respiratory acidosis Positive pressure breathing cortisone and the administration of oxygen are helpful but with oxygen administration extreme caution is in order With chronic hypoxia the respiratory centers become insensitive to the stimulus of carbon dioxide and the hypoxia per se regulates breathing If it is abolished by the administration of oxygen respiration becomes too superficial and death results

Carbon dioxide narcosis causes confusion maniacal states drowsiness and coma Headaches and muscular twitching occur (Westlake et al)

Symptoms

There are no characteristic symptoms Only late when edema and hepatic enlargement appear is the attention of the patient and the physician directed to the heart Usually in the early stages such symptoms as dyspnea and palpitation seem fully explained by the basic pathology in the lungs the lesser circuit or chest wall Most of these patients die before the right ventricle fails owing to the underlying disease This holds not only for patients with emphysema fibrotic tuberculosis and so forth but also for those with kyphoscoliosis (respiratory failure)

Anginal Pain Patients with cor pulmonale have two complaints which are of great interest *One is pain of an anginal character with typical radiation* into the arms which may sometimes be relieved by nitroglycerin This pain occurs in mitral lesions pulmonary embolism asthma and emphysema In one of our patients a 58 year old man with this type of pain often excruciating death occurred in a paroxysm necropsy revealed rupture of the main stem of the left pulmonary artery presumably the result of paroxysmal hypertension in the lesser circuit The rupture extended to the adventitia and was 1½ cm long An hematoma was found in the pulmonary hilus

Fainting *Another complaint is the appearance of effort syncope or tussive* syncope that is attacks of fainting during exertion or paroxysms of cough This event is also seen in congenital heart disease particularly in primary pulmonary hypertension The incidence in the latter group was 20 per cent (Dressler) Before fainting the patient experiences dizziness epigastric fullness a tight sensation over the heart and choking The systemic blood pressure falls and sinus bradycardia appears The patient loses consciousness when the blood pressure reaches a particularly low level In older literature similar syndromes were known as ictus laryngeus and in 1876 Charcot described laryngeal vertigo (laryngeal epilepsy) For many years epilepsy was assumed to exist in such cases since tonic clonic convulsions occur during this syncope One of the explanations available is the assumption of a high intrathoracic pressure during paroxysms of coughing whereby the cardiac inflow and output are diminished to such a degree that fainting occurs Intrathoracic pressures of 200—300 mm Hg have been measured during violent coughing Laughter choking and the Valsalva experiment cause similar fainting According to McIntosh et al cough syncope is the consequence of the markedly increased intrathoracic and intraabdominal pressure which is transmitted to the cerebro spinal fluid so that blood is squeezed out of the cranium It seems that in certain localities eliciting this type of fainting is a game in which students indulge (Howard et al) Lethal accidents during this type of fainting have been reported and are said to occur in one to two per cent of the cases Sudden death in patients with cor pulmonale is known to occur often

Signs

A regular sinus tachycardia of 100—120 beats per minute is common. Arrhythmias are rare. While right ventricular hypertrophy is invariable, its existence usually cannot be proven by means of physical examination because the underlying pulmonary pathology often causes superimposition of the lungs over the heart (emphysema). For the same reason the heart sounds are distant and sometimes scarcely audible. The point of maximum intensity of the heart sounds is often near the xiphoid because the whole heart is covered by the lungs. Murmurs are more often absent than heard. A high pitched diastolic murmur over the pulmonary artery is occasionally audible and derives from a relative pulmonary insufficiency (Graham Steell murmur). A gallop rhythm may be audible over the right ventricle.

In view of these difficulties x ray examination is indispensable for diagnosis, although here also difficulties are encountered. The form of the heart often cannot be determined in patients with chest deformities (e g kyphosis) and it may be equally hard to judge its size. Mitral configuration is common due to displacement and rotation. The displacement of the diaphragm likewise makes difficult any estimation of the size and shape of the heart.

The section of the right ventricle that is chiefly and in many cases exclusively altered is the outflow tract. The axis of this portion of the right ventricle runs almost perpendicular. Therefore dilation of the outflow tract leads to prominence of the conus at the left cardiac border and to filling of the cardiac waist. One reason for this is the resistance offered by the diaphragm whereby the outflow tract of the right ventricle finds it easier to dilate upward. If the diaphragm is low this resistance below is not encountered and enlargement of the conus therefore appears much later if at all (Zdansky). The mitralization is accentuated by rotation of the heart around its axis to the left a typical event in any right ventricular dilatation. The hypertrophy and dilatation of the outflow tract of the right ventricle even if considerable do not cause an enlargement of the cardiac shadow in the transverse diameter visible in the posteroanterior view. It is easily seen however in the left anterior oblique position.

Only late when the inflow tract of the right ventricle also dilates does the transverse diameter of the heart increase to make the heart seem enlarged. Since the right ventricle lies mainly in the left chest and in these cases forms a considerable part of the left cardiac border the heart appears enlarged to the left instead of the right even in advanced stages.

In pulmonary hypertension a systolic click may be heard over the pulmonary artery explained by the systolic tension of the wall of the pulmonary artery.

The systemic blood pressure is often low. A systolic blood pressure under 100 mm Hg is not unusual. No explanation of this finding is available at present. While its occurrence in tuberculosis has been attributed to a toxemia undoubt

edly some other mechanism is at work Spinal fluid pressure is often increased in emphysema and papilledema occurs (Flint)

Clubbing of the fingers and polycythemia are not rare

The electrocardiogram shows right axis deviation and later evidence of right *ventricular strain Characteristic changes are found in the P waves they* are very low in lead I and abnormally high but not widened in leads II and III (figure 8b) The reason for these changes and the relation to cor pulmonale is not fully explored at present but the pattern is very common in this syndrome and is typical of it

The pulmonary artery and its main branches are usually dilated Although cyanosis and dyspnea are often present in most cases they are due to the underlying lung pathology The cyanosis is marked and may reach an unusual depth if a secondary pulmonary sclerosis develops or an open foramen ovale exists In advanced stages of pulmonary pathology there is decided anoxemia and often hypercapnia The patient may have an overwhelming desire for sleep Not uncommonly the patient becomes continuously drowsy and may die in semi coma which has lasted for days Convulsions may appear terminally

The liver enlarges slowly and therefore is not tender The edema rarely reaches the degree encountered in the valvular and myocardial diseases These patients usually develop a form of high output failure

Differential Diagnosis

As a rule this is not difficult Clubbing of the fingers and toes marked cyanosis and the presence of a systolic murmur over the heart may suggest a congenital heart lesion in some cases Therefore the distinction is not always as easy as one might guess characteristic murmurs like other pathognomonic signs may be absent in congenital anomalies a secondary emphysema may be found in any cardiac patient A careful examination and evaluation of all findings make possible a correct diagnosis in most cases

The most frequently overlooked cause for chronic cor pulmonale is chronic pulmonary embolization If this picture lasts over many months without pulmonary infarctions and hemoptysis patients develop evidence of congestive heart failure (edema liver enlargement venous congestion) and are treated as instances of coronary disease with failure Anticoagulants or ligation of the vena cava inferior saved lives in several of our patients The diagnosis is missed since the lower extremities need not show any evidence of abnormality the emboli coming from deep thrombi of the legs or from the pelvic veins

Treatment

The therapy is that of the underlying disease Only symptomatic treatment is available for the cor pulmonale syndrome itself Once full decompensation with hepatic enlargement and edema occurs compensation can rarely be re established by therapy

The hypoxemia resulting from the pulmonary disease contributes to this futility of treatment Oxygen under pressure may be life saving In recent years since antibiotic therapy and aerosols have been available considerable help can be given to patients with chronic bronchitis and even to patients with right heart failure — they may become compensated again if careful attention is paid to the treatment of the lung thus abolishing the hypoxia and high pulmonary arterial pressure It has also been pointed out (Moe and Visscher) that the increased load on the right ventricle increases intraventricular tension and that this impairs the blood supply to the right ventricle via the coronary arteries This could also disturb the blood flow through the thebesian veins Moreover increased intra atrial pressure hampers the outflow of blood from the coronary sinus vein

Diamox can be of help in patients with cor pulmonale and retention of carbon dioxide

Sudden death without apparent cause is frequent in these cases as mentioned above Often cardiac decompensation begins insidiously and progresses slowly so that death is the result of the underlying pulmonary disease or secondary infections

In view of the respiratory disturbances so common in these patients breathing exercises with particular reference to the use of the diaphragm are of primary importance in the prolongation of life (Hofbauer Schutz Barach) As mentioned above many of these patients die a pulmonary death (respiratory insufficiency)

While digitalis should be given in the presence of decompensation its results are rarely spectacular unless the other measures mentioned above are used

The injection of morphine is absolutely contraindicated and may lead to sudden death (see last chapter) Demerol is permissible if given cautiously

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Chapter 20

Hypertension

General Remarks

Definition

In one of the first clinical studies on blood pressure von Basch considered a systolic blood pressure of 150 to represent the upper limit of the normal level A diastolic blood pressure of 100 has been considered as the upper normal diastolic blood pressure

A study by the Joint Committee of the Association of Life Insurance Medical Directors of America showed however that values above 140/90 mm Hg are definitely abnormal at any age (Daley et al) The frequently expressed opinion that higher values may be expected in elderly people and that they lack significance is not valid The blood pressure of a normal individual does not necessarily increase with age to a degree that it becomes higher than 140/90 mm Hg Papers with a dissenting opinion appear from time to time but the life expectancy of patients with a blood pressure above 140/90 is decidedly shorter than in those with lower pressures Sometimes particularly in younger subjects there is an elevation only of the diastolic blood pressure the systolic remaining within normal limits The diagnosis of hypertension in such cases is justified

A temporary moderate rise of blood pressure is observed in juveniles An examination of 6000 male university freshmen disclosed a blood pressure in excess of 140 mm Hg in 22 per cent (Alvarez et al) This elevation of the blood pressure in juveniles is best explained by an endocrine imbalance

Significance

Arterial hypertension ranks high among the causes of death more than any other disease it is responsible for cardiac symptoms and signs

Hypertension directly accounts for 15 per cent of deaths in patients over 60 years of age It is estimated that between the ages of 40 and 49 a blood pressure of 150/90 mm Hg or higher occurs in more than one fourth of males and one third of females Fifty per cent of the population over 50 have hyper tension

An increase of the blood pressure with age has been repeatedly reported (Master et al Hamilton et al) but this does not prove that a pressure over 150/90 is not abnormal at any age According to Master in men between the

ages of 50 and 54 the blood pressure may vary between 115/70 and 160/98 normally In men between 60 and 64 it is 190/110

Pickering found the mean systolic and diastolic blood pressures of males between 15 and 19 years old to be 117 2/68 2 while it was 117 2/70 8 in females of the same age Between the ages of 35 and 39 it was 125 2/77 8 and 127 5/79 3 respectively Between 65 and 69 it was 152 1/85 2 in man and 172 9/94 1 in women These figures illustrate the well established fact that with advancing age the incidence of hypertension is greater particularly in women To conclude that a blood pressure of 172/94 in an elderly subject is normal because it is a common finding is in our opinion wrong With increasing age pyorrhea is more common Should we therefore conclude that pyorrhea is normal?

About 140 000 deaths occur annually from hypertension and its consequences in the United States (G Fahr) The great incidence of hypertension in young men examined by the Army draft boards made it the second most common cause for rejection and this has raised questions about the evaluation and prognostic significance of a moderate elevation of blood pressure

Technique of Blood Pressure Determination

The blood pressure should always be determined by auscultation and by palpation In view of the many disagreements regarding the correct method for measuring the blood pressure a Committee of the American Heart Association and the Cardiac Society of Great Britain and Ireland made joint recommendations on this subject

The blood pressure should be obtained with the patient lying (British Committee) or seated (American Committee) The arm on which the pressure is taken should be flexed and should be supported at heart level on a smooth surface No constriction of the arm by clothing is permitted The blood pressure may be obtained by an aneroid instrument which must be calibrated annually but a mercurial instrument is more reliable The air vent in the mercurial instrument must not be permitted to clog The mercury at rest should reach exactly the *zero mark* and in the aneroid instrument the needle should stand exactly at zero The standard cuff *should have a width of 15 cm and should have a* rubber bag 12 to 13 cm in width and 30 cm in length Decompression should proceed at a speed of 2—3 mm per second The cuff should not bulge on inflation and the rubber bag should be applied to the inner side of the arm If possible smaller cuffs should be used for children and wider ones for measuring the blood pressure in the lower extremities The blood pressure should always be taken in both arms Several readings should be taken and the cuff inflated and deflated several times

The systolic blood pressure obtained with the auscultatory method is about 10 points higher than that obtained by the palpatory method It varies at different times of day and is higher after a meal or following excitement The blood pressure may be higher or lower in the right arm than in the left Differences between

the right and left arms are found in 76 per cent of normal subjects. Usually the blood pressure is higher on the right side. In 8 per cent of normal people the blood pressure was 20—30 mm Hg higher in the right arm (Amsterdam and Amsterdam). Greater differences are due to syphilitic changes at the mouths of the large arteries originating from the aorta, to mechanical compression by a cervical rib, to the scalenus anticus syndrome, or to the pulseless disease. Arteriosclerotic changes are rarely etiologic.

The level of the diastolic blood pressure is the point at which the sounds suddenly become muffled and dull. In cases of aortic insufficiency and other conditions with a large pulse amplitude, the exact estimation of the diastolic blood pressure may become impossible. The values obtained usually are too low. According to Gallavardin, the determination of the exact diastolic blood pressure is impossible in about 10 per cent of the cases.

When the readings of the systolic pressure by the auscultatory and palpatory method differ widely, the Committee recommends accepting the palpatory reading as more nearly correct.

In arrhythmias, particularly in atrial fibrillation, the estimation of the systolic blood pressure is difficult, and it is almost impossible to obtain correct values for the diastolic blood pressure.

In hyperactive hearts, the pulse wave may strike the cuff with such force that sounds are audible distal from the cuff in the cubital artery, and too high values of the blood pressure are obtained by the auscultatory method.

With small arms and the use of standard cuffs, the values of the systolic blood pressure are usually too low. With large arms, they are usually too high.

Like the temperature, the blood pressure in normal subjects varies constantly. It is lowest during sleep and in the morning. Transient rises are often forerunners of persistent hypertension.

Auscultatory Gap

A very important but little known source of error in the determination of the blood pressure with the auscultatory method is the so called silent zone or auscultatory gap.

With gradual deflation the sounds or murmurs (in the second phase of Korotkow) suddenly disappear, and with continued deflation they reappear and permit the estimation of the diastolic blood pressure. One may find, for example, that the sounds appear at 200 mm Hg, vanish at 180, then reappear at 130 and disappear completely at 100. The blood pressure of this patient is 200/100, but between 180 and 130 no sounds or murmurs are audible over the cubital artery. If the cuff had been accidentally inflated only to 160 and then the pressure slowly released, sounds would have appeared at 130 and disappeared at 100, so that the blood pressure would have been considered 130/100 mm Hg. Serious errors are avoided if the systolic blood pressure is always determined by the palpatory method as well as by auscultation. The auscultatory gap is more

distinct or may appear only when the cuff is held under pressure for some time (Pines and Scherf)

That the level of the venous pressure has some importance for the occurrence of this phenomenon is revealed by another experiment The gap may be found if the blood pressure is obtained with the arm hanging down and disappears if the arm is elevated (Berry) It may exist only in the right or only in the left arm In some patients it is transient while in others it is observed for weeks The auscultatory gap has been found in 10 per cent of hypertensives (Amsterdam and Amsterdam) Apart from those with hypertension it is *frequently encoun tered* in connection with stenosis of the aortic valve (Gallavardin and Tixier) It occurs however in nonhypertensives and also in the absence of aortic valve lesions

In some cases of hypertension and particularly when the cuff remains inflated for a while auscultatory phenomena above the gap disappear completely or are present only for a few millimeters so that the physician who deflates the cuff quickly overlooks this phase completely

Cold Pressor Test

The cold pressor test recommended by Hines serves to find an abnormal response of the blood pressure to an external stimulus At first the basal blood pressure is measured with the patient resting in the supine position for 20 to 60 minutes While the cuff is still on one arm the opposite hand is immersed in ice water (4° Celsius) up to the wrist and the blood pressure is again measured 30 to 60 seconds later The higher reading is recorded as the response The hand is then removed from the ice water and the blood pressure is taken every two minutes until it returns to the basal level No vasodilator or sedative drugs are permitted for 24 hours before the test

Elevation above the basal level of more than 20 mm Hg of the systolic pressure and more than 15 mm Hg of the diastolic pressure indicates a hyper reactor Such a hyper reactor is in greater danger of developing hypertension than normoreactors In normoreactors the blood pressure values return to normal within two minutes after the hand is removed from ice water This is delayed in hypertensives or in patients who are hyper reactors Pickering denies the clinical value of this test

TYPES OF HYPERTENSION

The blood pressure may be increased in a great variety of conditions some of which were mentioned in previous chapters The cause of the abnormal blood pressure is known in approximately 5 per cent of patients with hypertension In the remaining 95 per cent the blood pressure is high without any visible cause or known reason This type of hypertension is called essential hypertension a common but extremely unsatisfactory term that reveals actually an ignorance of the etiology It is probable that the group of patients to whom this phrase is applied will decrease steadily in coming years

Theoretically hypertension may appear (1) with changes of cardiac dynamics (increased contractility) (2) with changes of conditions of the large vessels (aorta) (3) with increased volume of circulating blood (4) with increased viscosity of the blood (polycythemia) or (5) with a narrowing of the peripheral vessels (arterioles) We shall see that instances exemplifying most of these mechanisms are known but that the last mentioned narrowing of the arterioles is present in an overwhelming number of cases

Hypertension is known to occur in certain endocrine disorders in certain disturbances of cardiac action in nervous disorders and in renal diseases and some affections of the urinary passages

1 Hypertension in Endocrine Disorders

Hypo ovarianism The most common cause of hypertension in this group the natural or artificial menopause has been discussed earlier Peference was made to the markedly fluctuating and in later stages even fixed hypertension in women with disturbed estrogen formation it is not a lack of estrogen but the endocrine imbalance in connection with it that seems to elevate the blood pressure in these cases The syndrome of hypertension and tachycardia in women between the ages of 40 and 50 years certainly is often due to this imbalance We have mentioned earlier that many authors consider hypertension in women of this age group as coincidental but this does not concur in our experience

Adrenals Primary aldosteronism with adrenocortical hyperplasia hypo kalemia and hypernatremia causes hypertension The frequency and patho genesis of this complication is not clear (Conn Chalmers et al) Patients with potassium losing nephritis seem to belong in this group According to Genest hypertensive patients secrete larger amounts of aldosterone than normals In primary aldosteronism in addition to the hypertension hypokalemia alkalosis and a tendency to hypernatremia exists Attacks of muscular weakness (inter mittent paralysis) are presumably due to the hypokalemia Diarrhea is common

Enteramine Serotonin These hormones secreted by the argentophile cells of the large intestines play an important but not yet fully analyzed part in the genesis of hypertension While the effect of 5 hydroxytryptamine on the blood pressure is erratic tryptamine without the hydroxy group causes hypertension The 5 hydroxytryptamine seems to regulate vascular tone and constricts the *afferent glomerular blood vessels* (Erspamer)

Pheochromocytoma

PATHOLOGY While this lesion was occasionally observed by pathologists no clinical description was available until 1922 The lesion consists of a usually benign rarely bilateral tumor composed of mature chromaffin cells of the adrenal medulla or other chromaffin bodies The new growth is encapsulated and may be malignant functioning metastases occur The tumor may weigh a few grams or as much as three kilograms and may also occur in the chest or cranium

INCIDENCE The tumors occur with equal frequency in both sexes and may develop in several members of the same family Poth et al saw them in two sisters and one brother They are most common in younger individuals

SYMPTOMS AND SIGNS In many patients the symptoms are typical The complaints consist of sudden attacks of palpitation with tremor dizziness and chest pain Anginal pain is present in almost 50 per cent of the patients during an attack of hypertension Severe headache and epigastric pain are also common Nausea is often present The systolic blood pressure may rise from 110 to 300 or more and the diastolic from 60 to 140 or more Often with the rise of blood pressure bradycardia or arrhythmias develop Glycosuria and albuminuria frequently develop during an attack Circumoral pallor and pallor of the cold and mottled extremities may be found although in many patients the face is flushed

The diagnosis is often possible on the basis of the history One of the most common complaints is a very severe definitely pathologic headache There may be also abdominal pain particularly in the epigastrium so that an acute abdomen may be simulated There is tingling in the hands and feet occasionally violent palpitation with strong pulsation of the vessels in the neck and anxiety Vomiting blurring of vision or even amaurosis appear The skin is often cold and covered with perspiration after the attack great fatigue and lassitude may occur Pulmonary edema may appear causing collapse and even death In some patients it produces a complaint of a sinking sensation Patients may develop a cerebral vascular accident during the attack

Permanent hypertension may be found without a history of attacks The incidence of this picture is not definitely known for statistical data vary According to Organ it is responsible for 0 47 per cent of hypertension Other authors considering only patients in whom tumors were found give a much higher incidence This syndrome should be particularly suspected when there is hypertension glycosuria and a marked increase of the basal metabolic rate One should bear in mind that hypertension of any etiology persisting for a time may become permanent either experimentally or clinically

The hypermotility of the heart resembles that seen in hyperthyroidism The differential diagnosis from the latter condition is often difficult since these patients often have a markedly increased basal metabolic rate Like hyperthyroidism patients of this kind also have an intolerance to heat slight glycosuria after a prolonged attack may cause the physician to diagnose diabetes In prolonged attacks the temperature is increased The electrocardiogram during the attack may show marked abnormalities of the T waves ventricular extrasystoles and even tachycardias Sometimes the attacks cause so little distress that the patient does not seek medical advice other times the episodes are so incapacitating that medical counsel is a necessity

Since the investigations of Goldenberg and his associates were published it is now established that not only epinephrine but also norepinephrine (in some tumors only this substance) are excreted by the tumor into the circulation

In patients with large tumors bending forward suffices to expel these compounds into the circulation and to provoke an attack This secretion of noradrenaline causes changes in the potassium content of the blood which in turn may be responsible for the cardiac arrhythmias observed during the attack The clinical symptoms and signs vary since in some patients more epinephrine while in others more norepinephrine is secreted

The attacks may last for minutes or hours They may occur at any moment but they are prone to develop at a fixed time often at night Years months or hours may pass between single crises Sometimes it may be possible to provoke an attack by pressure on a palpable tumor which is most often situated on the right side squatting exposure to cold or excitement may also provoke an attack Attacks may appear after exercise Sometimes there is a time relation to the previous meal or excitement

LABORATORY TESTS In addition to the old diagnostic tests — intravenous pyelography and perirenal or better presacral air insufflation now improved by the replacement of air by oxygen laminography and the like — new tests are available Occasionally they may lead to false positive results but in general they are reliable and facilitate the diagnosis False positive results are obtained most often when one tries to provoke an attack by an intravenous injection of 0 025—0 05 mg of histamine In the presence of a pheochromocytoma this causes a marked rise of blood pressure in a few minutes The histamine test may be used when the resting blood pressure is not over 150/110 False negative tests do occur A rise of systolic blood pressure by 60 mm Hg or more and of the diastolic by 30 mm Hg or more is significant

Goldenberg s benzodioxane test is performed by the intravenous injection of 10—15 mg of this substance for the regitine (phentol amine) test 5 mg of regitine are used These substances counteracting the action of epinephrine and norepinephrine cause a definite fall of pressure in a few minutes after the injection in all subjects who have a blood pressure elevation due to pheochromo cytoma False positive tests appear after sedation with barbiturates and Rau wolfia drugs and in uremia At the present time it is assumed that regitine causes fewer side effects than benzodioxane and should be preferred for the test In patients with hypertension in the absence of a pheochromocytoma benzo dioxane may cause a marked rise of pressure (Fremont)

At present the excessive urinary excretion of catechol amines determined by photometric methods seems to be the most reliable test A 24 hour specimen is assayed

Operative procedure of any type particularly removal of the pheochro mocytoma may cause shock Postoperative patients require careful super vision Metastases may be functionally active

Cushing s Syndrome Hypertension appears in the adrenal cortical syndrome which is characterized by marked obesity particularly of the abdomen hir sutism purplish striae hyperglycemia and osteoporosis This syndrome formerly attributed to basophilic adenoma of the anterior hypophysis (Cushing s

spaces in which blood could potentially be stored) are not available in patients with generalized edema because the edema compresses peripheral veins The circulating blood volume being markedly augmented leads to an overfilling of the large veins and an increased cardiac filling and to an increase of the systolic and diastolic blood pressure With a marked diuresis (often following only *one* injection of a mercurial diuretic) the peripheral blood depots become available blood is again stored the amount of circulating blood decreases and the blood pressure falls (Goldhammer et al)

It is not always possible to restore compensation fully and therefore this hypertension may not be reversible and the blood pressure may remain high despite therapy

Since patients with congestion of the kidneys may show marked albuminuria and casts in the urine mistakes in diagnosis are common It should therefore always be remembered that hypertension occurs in congestive heart failure and is often the consequence of decompensation it does not always mean a renal or vascular disorder

3 *Hypertension in Nervous Disorders*

The influence of the central nervous system on blood pressure was widely discussed at one time but had been somewhat neglected until recently In the last few years this question has again attracted considerable attention (Raab) particularly since the discovery of the carotid sinus reflexes demonstrated the importance of a nervous regulatory mechanism for the blood pressure level

This form of hypertension is accompanied by an increase of rate The increase in cardiac output is claimed to be the chief reason for the hypertension

An increase of intracranial pressure may lead to hypertension most probably because the intracranial vessels are compressed and the centers rendered anemic Prolonged hypertension can be produced experimentally by the injection of kaolin into the subarachnoid space (Dixon and Heller) when it spreads to the cerebral ventricles and by experimental creation of cerebral ischemia Clinically hypertension is observed in brain tumors and in vascular disease causing cerebral ischemia

Hypertension also results when all four moderator nerves (right and left carotid sinus nerves and right and left aortic depressor nerves) are severed This is due to the disturbance of homeostasis and the release of vasoconstrictor centers which are normally inhibited

Cases of encephalitis bulbar poliomyelitis and concussion of the brain and trauma to the midbrain with paroxysmal hypertension have been observed

The importance of fear anxiety and apprehension in the causation of hypertension is also well known This increase of blood pressure stems from the release of adrenalin and noradrenalin and stimuli running from the emotional to the vasoconstrictor centers The importance of these factors in the development of essential hypertension will be discussed later

The Hypertensive Diencephalic Syndrome This form of hypertension described by Page is most often found in middle aged women Such subjects exhibit great emotional instability blush in spots and show red patches on the neck and chest The extremities are cold pale and clammy The neck vessels pulsate strongly The blood pressure is labile and may temporarily reach high values The heart is normal in size and shape for many years and the electro cardiogram does not show any change demonstrating that the blood pressure is not fixed and often reaches normal levels The syndrome resembles attacks seen in connection with organic diseases of the hypothalamus An increased response to 0 25 ml of a standard histamine acid phosphate solution was described in this condition Dermography is common

4 Hypertension in Renal Disease and in Diseases of the Urinary Passages

The occurrence of hypertension in renal disorders is so common that an increase of blood pressure has been considered by some authorities of the past (and is considered even today) to mean an involvement of the kidneys

Humoral Mechanism The mechanism of increased blood pressure appears to have been greatly clarified by recent investigations but is however much more complicated than it seemed at first It must be stressed that the mechanism of hypertension of renal di eases is still unknown there is no proof that a humoral mechanism is responsible

A humoral mechanism in the production of hypertension was suggested by Tigerstedt and Bergmann who isolated a pressor substance from the kidneys Although confirmed these experiments rarely received correct evaluation until Goldblatt demonstrated that constriction of the renal arteries in dogs under certain conditions causes persistent hypertension This hypertension may lead to renal changes identical to those seen in human malignant hypertension The kidney whose artery is clamped does not show these changes indicating that they are secondary to the hypertension Complete sympathectomy does not prevent this hypertension nor is normal blood pressure restored by the operation if hypertension existed (Freeman and Page) Pemoval of both adrenals causes the blood pressure to return to a normal level (Goldblatt) It was su pected (Hartwich) and later demonstrated that the ischemic kidney releases a sub stance identical with rennin Pennin is an enzyme that unites with blood globulins to form a peptide hypertensin or angiotonin Pennin is probably formed by the cells of the proximal convoluted tubules Another enzyme is present in blood and ti sues (hypertensinase) which quickly destroys hypertensin The normal kidney is able to counteract the pressor effect of the pressor substance formed by an ischemic kidney

Deamination According to others the pressor amines formed during normal metabolic processes are not deaminized by the ischemic (anoxic) kidney and these circulating amines cause hypertension

Kidney Diseases In acute and chronic nephritis pyelonephritis periarteritis nodosa and polycystic kidney hypertension is common but not obligatory so

long as no nitrogen retention exists The reason for the hypertension is unknown Even the hypertension in coarction of the aorta has been explained by a diminution of renal blood supply

It has long been known that hypertension appears in obstruction of the urinary passages and may disappear if the obstruction is removed Hypertension occurs in prostatic hypertrophy in hydronephrosis and in ureteral stone A diminished renal blood supply due to attenuation of the renal vessels is produced by stretch and compression in such cases

Hypertension appears in unilateral compression of the main renal artery by a tumor glands or an abnormality of the vessel It appears in unilateral pyelonephritis or renal embolism In many instances of unilateral kidney pathology removal of the affected kidney abolished the existing hypertension (Howard) As might be expected these operations are not always successful since experimental studies show that a hypertension persisting for a long time leads to secondary vascular changes in the other kidney therefore the hypertension is maintained even if the initiating factor is abolished There is a greater probability of a fall of blood pressure following nephrectomy in these cases if the hypertension is less than two years old Poutasse et al report on hypertension caused by bilateral stenosis of the renal arteries in three patients fourteen fifteen and twenty five years old In one of these patients homografting of both renal arteries abolished the hypertension According to Schaffer and Markowitz nephrectomy in patients with unilateral kidney disease brings a cure in ⅓ of the patients and does not cause any improvement in another third

Despite the fact that urologic hypertension is not common a careful history must be taken and intravenous pyelography should be performed in *every* patient with hypertension of unknown etiology (negative family history) in order to rule out kidney pathology If this is done urologic hypertension will be discovered in patients whose history and physical examination arouses no suspicion of the presence of this condition

The fact that dorso lumbar sympathectomy may diminish hypertension markedly in patients with renal diseases is not compatible with the assumption of a purely humoral mechanism in these cases

Eclampsia (and pre eclampsia) This combination of edema (gain in weight!) hypertension and albuminuria with convulsions coma and death has an unexplained pathogenesis Pennin has however been found in the blood Hyperadrenalism was considered possible Toxemia of pregnancy — a term still in use today even if somewhat out of order and inaccurate — appears more readily in patients with renal disease The syndrome appears in primiparas in the seventh and eighth month but if hypertension already existed it appears earlier more frequently and is more severe Headache nausea and drowsiness often precede eclampsia These attacks like attacks of hypertensive encephalopathy are elicited by the high blood pressure (Byrom)

Sometimes hypertension does not increase during pregnancy but this is not common

Kimmelstiel Wilson Syndrome This syndrome is found in diabetics It consists of albuminuria retinopathy a nephrotic type of edema hypertension — and later azotemia Some of these signs are missing at times The diabetes is often mild The syndrome may also be found in juvenile diabetics It appears after the diabetes is present for 8 to 10 years Death usually occurs in 6 or 7 years A characteristic finding is the presence of hyaline deposits in the glomeruli The urine shows double refractory lipoid droplets There is no specific therapy The mechanism of the hypertension is unknown

Essential Hypertension

Definition

As pointed out before essential idiopathic hypertension is diagnosed when all known causes of hypertension are excluded Since the introduction of pyelography with contrast media cases of hypertension are discovered to result from otherwise unsuspected kidney pathology Progress in endocrinology has helped to explain other instances of hypertension All these and the other types of hypertension mentioned however represent the exceptional case — about 95 per cent of patients under 50 years of age with an increased blood pressure belong to the essential type It is undetermined whether we are confronted with a disease entity and it is hoped that more types of hypertension with known mechanisms will be separated from this large group Until the different forms are recognizable we are in favor of retaining this useful term

Inconsistencies in the concept of essential hypertension were pointed out by Raab (1955) According to Pickering (1955) essential hypertension represents the upper end of the distribution curve of blood pressures observed in our population Essential hypertension is not qualitatively different from normal pressure Patients with a blood pressure higher than an arbitrarily selected level are separated as a group with essential hypertension

Incidence

Sex Age Essential hypertension seems to be slightly more common in women than in men Possibly the figures would be different if all hypertensions due to previous toxemia of pregnancy and to the menopause were excluded It occurs at all ages It has been described in a two year old boy in whom it caused progressive heart failure It is not rarely encountered in juveniles or adolescents with essential hypertension in their families particularly with both mother and father suffering from the disease The temporary moderate increase of blood pressure in juveniles which has been mentioned earlier must be kept in mind

The great incidence of hypertension of all types in the general population was discussed above The figures given are also important for evaluating the incidence of essential hypertension if the relation of this form to other types of high blood pressure is remembered

Race It seems established that Negroes living in Africa and Chinese in China rarely have hypertension although they do develop it in the United States with the same frequency seen in the white population (Schwab and Schulze) This difference is significant for it shows that it is not the race but the mode of living and perhaps the type of food which is important

Heredity The frequent occurrence of essential hypertension in several members of the same family is established Essential hypertension is inherited as a dominant characteristic In families whose members have an absolutely normal blood pressure the incidence of an elevated arterial pressure in the offspring is 3 1 per cent If one of the parents has hypertension the incidence rises to 28 3 per cent and in families in which both parents are so affected the incidence is 45 5 per cent In securing the family history it does not suffice to ask whether hypertension or heart disease have occurred in close relatives Since most of the patients do not know that a stroke dropsy angina pectoris or cardiac failure are often consequences of hypertension they answer in the negative For this reason it is better to seek the actual causes of death in the previous generation

It seems that the increase of blood pressure is observed in a progressively younger age group with each generation of a hypertensive family

Constitution The role of constitutional factors has often been discussed Males suffering from hypertension often present the sthenic habitus they are short stocky individuals with a short thick neck and a deep chest On the other hand females often appear frail Exceptions to this rule are however not uncommon Patients of both sexes are frequently obese and diabetes is common in their families

Pathology

In early stages of the disease no abnormal findings are discovered in spite of complete postmortem examination Previous reports dealt with single cases because patients do not often die from this disease at an early stage These observations were confirmed by many biopsies obtained during sympathectomy for the treatment of essential hypertension Hypertension antedates the renal vascular changes (Castleman and Smithwick) In 28 per cent of the cases in which a surgical procedure seemed necessary no changes or only insignificant ones were found in the kidneys

With longer duration of the hypertension the number of patients with abnormal vascular findings increases in persistent hypertension arteriolosclerosis is a more regular finding The kidneys show an irregular granular surface and are contracted There is a focal arteriolosclerotic atrophy with hyalinization of the glomeruli and atrophy of the tubules Similar arteriolosclerotic changes are seen in the spleen liver heart and pancreas

Whether arteriolar sclerosis is a necessary sequel in every hypertension has not been established beyond doubt It does not occur in cases of coarctation of the aorta or in experimental neurogenic hypertension

Etiology and Pathophysiology

The mechanism underlying the development of hypertension of the essential type *is unknown*. It *is possible that many* factors contribute and that there is more than one etiologic agent.

A small minority of physicians still believes that *humoral mechanisms* are responsible. But hypertensin has not been found in the blood even in the renal vein of hypertensives; it was found only in eclampsia and in hypertensive crises. *There is no proof that other pressor amines are responsible.* This *holds in particular* for norepinephrine which, more than any other substance, when injected intravenously imitates the clinical picture of essential hypertension, since the cardiac output and cardiac rate is not increased. Actually only one pressor substance has been found *increased*, namely pherentasin (Schroeder), which has been isolated from the arterial blood of hypertensives. Its importance as a responsible agent is undecided. The same holds for the vasoexcitor material (VEM) discovered by Shorr and his collaborators. It has been isolated in humans and is found in *increased amounts* in hypertensives. *Its composition is unknown*. It is *formed* in the kidney under anoxic-ischemic conditions. Simultaneously vasodepressor material (VDM) which has been recognized to be the protein ferritin is formed in the liver. Like renin — from which VEM can be differentiated — it does not *cause hypertension directly but is said to sensitize the vessels to epinephrine*.

During the administration of desoxycorticosterone, ACTH and cortisone, hypertension may occur. Abnormal adrenal function may be responsible in other unknown ways. In this connection the occurrence of hypertension in aldosteronism is of interest.

Selye *considers hypertension to be a disease of adaptation. During stress* large amounts of corticotropic and corticoid hormones are discharged. Stress may cause hypertension and renal changes similar to nephrosclerosis. An excessive adaptation mechanism is said to lead to the clinical picture of hypertension. The hypertension in Cushing's syndrome, the necessity of the function of the adrenal glands for the maintenance of experimental hypertension, and the hypotension of Addison's disease show the importance of the adrenals. Details cannot be evaluated as yet.

According to some authors the kidney maintains a normal blood pressure by inhibiting extrarenal pressor mechanisms. Nephrectomy therefore increases the blood pressure. This extrarenal pressure mechanism may be located in the adrenal cortex.

According to Volhard, hypertension is caused by a decreased distensibility of the aorta and carotid arteries leading to an excitation of the receptors of the depressor nerves with higher pressure levels. A similar mechanism is discussed by Kedzi who found the excitability *of the receptors of the depressor* nerves and the depressor reflex to be normal. Nervous tension causes a rise of blood pressure which in turn produces less stimulation of the pressure regulating nerves in those with a *hereditary* tendency to degenerative processes in the arterial wall and

changes of the elastic fibers Heymans also considers a decrease of tonus and resistance to stretch of the supra aortic arterial wall as the primary mechanism of hypertension

It seems certain that *nerve tension* causes a rise of blood pressure Thus Graham found 187 subjects with hypertension among 685 soldiers in an armored brigade during the last war who had experienced at least one year of desert warfare with great excitement and stress The mean blood pressure was 178/114 mm Hg In 38 per cent a systolic blood pressure of 160 or more was found and in 26 9 per cent the diastolic pressure was 100 or over Out of 33 patients with hypertension the pressure returned to normal in 28 within two months after the excitement ceased

In the Texas City Disaster in 1947 Ruskin found hypertension in 103 out of 180 patients examined Injury of the hypothalamus causes hypertension hypertension was provoked in rats by audiogenic stimuli (Medoff and Bongiovanni)

The frequency of nervous hypertension (anxiety hypertension) is indicated by *its presence in 14 per cent of 1574 applicants at a military procurement office*

The fact that many emotions great mental strain, rage and anxiety cause a temporary hypertension is further evidence of the role of a nervous mechanism in the development of essential hypertension A hyperexcitable sympathetic system an abnormal vascular response to physiologic stimuli or an abnormality of the vasomotor centers (Raab) may be responsible Spinal anesthesia may cause a fall of blood pressure to almost normal levels in hypertension

The incidence of persistent hypertension seems greater in those who have had a transitory elevation of blood pressure in their youth

A certain type of personality is said to be common in patients with hypertension Such patients are very active great planners very dynamic and quick in every action They talk fast and give an excellent history They undress quickly for examination eat rapidly never walk but run One must concede however that at times patients with essential hypertension belong to the quiet slow deliberate type and seem exactly the opposite to the patients just described

Certain other personal traits have been found to be common There is great perfectionism and a subnormal assertiveness Emotional instability and compulsive tendencies exist There is often maladjustment Schroeder considers essential hypertension to be a psychosomatic disease

A combination of several of the above mentioned mechanisms is possible and even probable

An abnormal or individually exaggerated response of the autonomic nervous system to the normal excitements of daily life leads to a temporary slight narrowing of the peripheral arterioles and to transient hypertension Narrowing of the vessels in the central nervous system may prolong and accentuate this hypertension since the reduction of the cerebral blood supply causes chronic hypertension Constriction of the renal vessels and stimulation of the adrenal cortex accentuates and prolongs the bouts of hypertension by the formation of pressor substances and production of pressor hormones A vicious cycle develops (Wilson and Byrom)

Thus the following formula may be real nerve stimuli act on the hypothalamus which *in turn increases the tonus of the sympathetic system* This leads to renal ischemia and to greater peripheral resistance because of vasoconstriction which is in part humoral Sooner or later there are anatomic vascular changes in the arterioles since this part of the circulatory system offering the chief resistance is subject to the greatest stress in hypertension it causes a drop of blood pressure from the high level in the arteries to the low one in the capillaries

Symptoms

In most of these cases hypertension even when marked causes no symptoms whatever The increased blood pressure is discovered accidentally on the occasion of a life insurance examination or a similar situation Many patients aware of a high blood pressure for many years deny any discomfort Understandably many patients *particularly the more sensitive and alert type* develop symptoms from the time they are informed of the existence of a hypertension They have symptoms because they *know* that they have hypertension Patients are known to have had a systolic blood pressure of around 200 mm Hg for more than 20 years without any complaints

Fatigue Some patients seek help because of increased irritability sleeplessness and fatigue The last mentioned symptom is not rare but its mechanism is unexplained *This fatigue is very distressing and is unrelieved by rest* The same symptom is also common in arteriosclerosis We are not aware of any simple reliable therapeutic agent for its relief Fortunately the fatigue which plagues many patients may disappear spontaneously for some time but sooner or later it reappears It often occurs without any evidence of cardiac failure

Irritability and Tenseness Many patients are tense they feel driven and despite an effort to do things more slowly and with less expenditure of energy *they are unable to put the brakes on* This *makes one believe that the great* irritability and restlessness are not the cause of hypertension but a feature of its clinical picture

Epistaxis Vertigo Occasionally epistaxis is of sufficient severity to necessitate hospitalization It is explained by changes in the capillaries of the nasal mucosa Tinnitus and attacks of vertigo are not rare Vertigo occurs on change of posture *and is sometimes so severe that the patient is unable to lift his head from the* pillow or to change position in bed

Headache This is one of the most common symptoms Often it is present on *awakening or early in the morning and vanishes after an hour or more* It may be occipital or frontal and tends to be symmetrical rather than unilateral It may have a migrainous character Strong pulsations of the meningeal arteries are probably responsible In most cases there is no parallelism between the height of the blood pressure and the severity of the headache Sometimes however the headache is decidedly more severe when the blood pressure rises and therapy which lowers arterial pressure abolishes the headache In malignant hypertension the headache may be due *to cerebral edema* and then is relieved by lumbar puncture Nausea

and vomiting may occur Sudden appearance of exceedingly severe headache is ominous

Loss of Weight In advanced stages of hypertension especially in patients with generalized arteriosclerosis a sudden inexplicable loss of weight often impels the patient to seek medical advice While it is generally believed that hypertension is more common in the obese the idea is by no means unanimous (Proger) However undernutrition as it existed during the siege of Leningrad in the last war does cause a fall of pressure In patients with hypertension obesity may aggravate the cardiac burden In patients without hypertension or cardiac disease a syndrome has been described consisting of obesity alveolar hypoventilation arterial hypoxemia with secondary polycythemia and pulmonary hypertension causing right heart failure Reduction of weight causes marked improvement (Kerr and Lagen Weil)

Other Complaints In the late stages when such complications as cardiac failure coronary atherosclerosis angina pectoris or cerebral vascular sclerosis develop the symptoms peculiar to these disorders appear

Pounding and palpitation on effort or at rest are common complaints With the onset of left ventricular failure nocturnal dyspnea and cough begin

Signs

Blood Pressure The chief sign is elevated blood pressure The blood pressure should be taken repeatedly with the patient in the recumbent position and the highest as well as the lowest values should be recorded The auscultatory values should be checked against those obtained by palpation and estimation should be made in both arms

If hypertension is found the physician should try to obtain the reading with the patient relaxed — for example after a good night s rest or after the administration of a barbiturate (0 2 Gm of sodium amytal) or a similar sedative

In essential hypertension the systolic and diastolic blood pressure are both elevated The value of the diastolic pressure is more important than that of the systolic Every value above 95—100 is very suggestive The systolic level may exceed 300 mm Hg and the diastolic may be higher than 180 but usually the systolic pressure is near 200 and the diastolic near 100 mm Hg

Palpation Physical examination starts with palpation of the peripheral arteries Hypertonus of the vessels may make the pulse scarcely palpable despite the hypertension With medial calcification the vessels assume a pipestem character

Palpation of the chest and the precordial area in particular reveals no characteristic signs in benign hypertension Marked hypermotility is palpated in malignant hypertension this may be due to the activity of pressor substances

Percussion and X ray Examination The heart may be of normal size and shape for many years It has been correctly pointed out (Raab) that hypertrophy and dilatation do not parallel the height of the blood pressure Other perhaps hormonal factors may play a role The left ventricle responds to increased aortic pressure with greater residual filling and therefore higher initial tension of the

muscle fibers causing secondary hypertrophy These changes involve the outflow tract of the left ventricle and cause downward displacement of the apex without enlargement of the transverse diameter Since the lower part of the elongated ventricle is hidden in the abdominal shadow negative x ray findings particularly with films taken in the postero anterior view in a patient known to have hypertension for many years are not rare In the course of the disease sometimes even



Fig 86 Aortic configuration of the heart and widened aorta in a 50 year old patient with hypertension

20 years after the onset the left ventricle also dilates in a transverse diameter and an aortic configuration appears (figure 86) Cardiac hypertrophy and dilatation *may assume great proportions and with the exception of patients with aortic* insufficiency the hypertensive heart may be the largest and heaviest encountered If the patient has a cor bovinum but no aortic insufficiency or hypertension it is probable that he once had hypertension which has since vanished

The development of pulmonary congestion coincides with the mitralization of the heart

The aorta is dilated in the early stages but it is a dynamic dilatation which is not demonstrable at necropsy Later with the appearance of atheromatosis

the dilatation becomes permanent This dilatation is diffuse but in the ascending aorta it fails to reach the degree usually seen in aortitis The descending aorta is also dilated in contrast to the situation usually observed in aortitis

The elongation of the aorta sometimes causes a pulsation that is palpable in the jugular notch The elongation also displaces the right subclavian and the innominate arteries upward in the neck so that abnormally strong pulsations may be found on the right side of the neck above the clavicles which may be mistaken for those of an aneurysm The upward displacement of the aorta and innominate artery shortens the distance between the orifices of the right carotid artery at the innominate and its entrance into the skull This leads to an ab normal course and even kinking of the right carotid (Brown and Rowntree) A similar kink may also produce an aneurysm like pulsating mass in the left side of the neck when the elongated sclerotic left carotid artery pursues an ab normal course (Parkinson et al)

Auscultation The heart rate is usually normal or slightly increased The first heart sound is accentuated at the apex and the second sound is abnormally loud over the aorta This accentuation is absent however in many cases even if obesity or emphysema the usual reasons for the absence of the second sound are not present The second aortic sound was found normal in 46 per cent of hypertensives (Cossio et al) With the increased fibrosis and the appearance of lime salt deposits in the aorta the second sound may assume a metallic, ringing character

A systolic murmur is often audible over the apex and the aorta Sometimes both murmurs originate in the aortic area and the systolic apical murmur is merely transmitted In patients with emphysema the aortic murmur may disappear when the aorta is covered by lung in this instance the murmur is audible only at the apex

Most often the aortic murmur is due to dilatation of the left ventricle and the widening of the aorta in the absence of dilatation of the aortic orifice a relative stenosis mechanism exists Later especially in elderly patients sclerosis of the aortic valves may be responsible The apical murmur may also be created by sclerosis of the mitral valve particularly its aortic leaflet Naturally both of these murmurs the result of valvular sclerosis also occur in elderly patients without *hypertension* *The murmur due to atheromatosis* is often mid systolic and accordingly is easily separated from the first heart sound

With the development of a more pronounced dilatation of the left ventricle a relative mitral insufficiency appears and with it a new loud blowing systolic murmur may be heard at the apex

Gallop rhythm and pulsus alternans are common findings in hypertensive patients with the onset of myocardial failure

A diastolic aortic murmur due to a relative aortic insufficiency is in our opinion extremely rare

Fundus Examination Examination of the fundi shows many abnormalities This examination has fundamental significance in establishing the degree of

vascular changes. It should be done frequently to watch the progress of alterations. The earliest change consists in a contraction (narrowing) of the arteries, but often even this is missed in early stages, so that the fundi are considered normal. With the development of arteriosclerotic changes new phenomena appear. The vessels become tortuous, the light reflex is wider, copper or silver wire patterns occur, the lumen of the arteries becomes irregular and venous compression is visible at crossings.

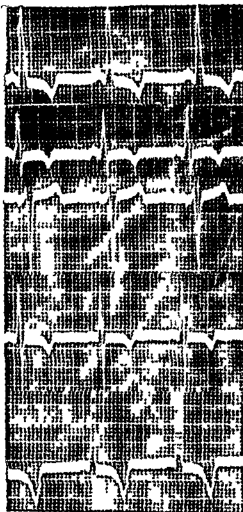


Fig 87. Pattern of left ventricular strain in a 58 year old woman with hypertension.

Hyaline deposits in the narrowed arterial walls cause the silver wire appearance. Even in the early stage, acute constriction of the arterioles may lead to exudates (cotton wool patches) and hemorrhages; these disappear readily when vasospasm (acute angiospastic retinopathy) relaxes. All atherosclerotic changes are occasionally found without elevation of the blood pressure.

With the development of very marked vasoconstriction and higher spinal fluid pressure, the optic disc swells and papilledema appears.

Importance of Retinal Findings. There have been repeated endeavors to differentiate several stages or grades of the disease. One method is based upon the retinal findings (Wagener and Keith). In the first grade the retinal findings are normal. This large group embraces those who have a normal blood pressure at rest and during sleep; moreover, they have few symptoms or signs. In the second grade some evidence of retinal vascular sclerosis is present, but none of hemorrhages or exudates. In the third grade, mild vasospastic retinopathy with hemorrhages and exudates exists but no papilledema. In the fourth grade, because of an increased spinal fluid pressure, papilledema is present in addition to the other changes. This hypertensive neuroretinopathy is always symmetrical. While this differentiation of the retinal changes is a great aid in evaluating the

status of the patient the prognosis depends upon many factors such as the status of the heart and brain

Leg Ulcers Ischemic ulcers of the legs are rare but do occur in hypertension (Martorell) they develop in the lateral supramalleolar region For the most part they appear in women between 50 and 70 who have had hypertension for many years Intimal proliferation is found in the arteries There is no specific therapy and the ulcers are slow to heal

Laboratory Findings In many cases the urine shows no albumin but in others albuminuria is very pronounced from the start Granular and hyaline casts also appear Sometimes the albuminuria is due to congestive heart failure

Examination of the blood urea nonprotein nitrogen and creatinin shows normal findings until there is destruction of the kidney parenchyma and renal ischemia The cholesterol level of the blood is occasionally slightly elevated The basal metabolic rate is frequently abnormal and even excessively high without any demonstrable thyroid involvement or existing cardiac failure

Electrocardiogram The electrocardiogram shows often left axis deviation this is however common in healthy subjects In late stages with the development of left ventricular hypertrophy and dilatation the RS T segment and T waves are displaced below the zero line in lead I (and often in lead II) while they are displaced upward in lead III This pattern of left ventricular strain is the same as that seen in aortic insufficiency (figure 87) The chest leads reveal more diagnostic changes In V2 leads the R waves may be absent and the S is deep in V5 there is a tall R wave, rarely followed by an S and the RS T as well as the T are depressed below the isoelectric line

In many cases of hypertension particularly in the advanced type with hypermotility of the heart a very short P R interval is found (Scherf) Thus in figure 87 in addition to the pattern of left ventricular strain a P R interval of 0 12 is present The conduction time often is even shorter This tracing was obtained from a 58 year old woman with a blood pressure of 210/120 mm Hg This shortening of the P R interval is by no means characteristic It is common in thiamin deficiency

Course

The tempo of the disease is subject to great variation Progress may be slow and a patient seen ten years after the first examination may still show the same findings At other times the course is stormy and the changes progress rapidly

Importance of Fixation of Blood Pressure From a purely clinical standpoint for many years two stages have been differentiated in patients with essential hypertension The first is the stage of fluctuating blood pressure values The examining physician finds a systolic blood pressure of 200 mm Hg in the first measurement If the determination is repeated in a few minutes after the patient has become adjusted and quiet the systolic blood pressure may be 160 mm Hg In this stage any excitement mental or physical exertion causes

a remarkable rise of blood pressure The innumerable impressions of daily life furnish sufficient occasion for maintaining the hypertension continually during the day During sleep or after the administration of sedatives after prolonged rest in bed the blood pressure is normal

After a variable period the stage of fixed blood pressure is reached Additional rise from excitement still occurs but neither sleep nor sedatives reduce the blood pressure to a normal level

By this time arteriolosclerosis may develop and the clinical picture as well as the course complications and prognosis depend on the degree of vascular changes in the different organs Circulatory complications are the most common renal complications are rare

Circulatory Complications These are manifold At least 50 per cent of the cases develop heart failure The progressive coronary sclerosis damages the myocardium which works under the heavy strain imposed by the hypertension this soon results in congestive heart failure In many patients, coronary sclerosis leads to angina pectoris on effort and myocardial infarction as the consequence of coronary occlusion It was noted earlier that hypertension is a common finding in patients with exertional angina and coronary thrombosis A small percentage of patients show evidence of obstructive atherosclerosis of the peripheral vessels of the lower extremities The early appearance of vascular complications does not depend on the height of the arterial blood pressure

The electrocardiogram may be very helpful in evaluating the progress of coronary sclerosis In addition to the left ventricular strain mentioned before slurring and widening of the QRS complexes (intraventricular block) and T wave changes may indicate the presence of coronary sclerosis The fact must be stressed however that marked coronary sclerosis need not cause any electrocardiographic changes under certain circumstances

Cerebral Complications Paralysis hemiplegia aphasia occur in 13 per cent of hypertensive patients In some cases these accidents are due to embolism from mural thrombi in the left ventricle More often they result from arterial thrombosis or hemorrhage or are due to cerebral edema Local vascular spasm (cerebral crises) are responsible for many temporary lesions (Byrom) The same mechanism causes the so called hypertensive encephalopathy

Headache and vertigo often precede cerebral vascular accidents for some time

In all probability cerebral hemorrhage is not the result of a simple rupture of an artery Experiments on cadavers show that a tremendous pressure (1 520 mm Hg) is necessary to rupture a cerebral artery Angiospasm causing local ischemia and therefore damage of vessels or damage of brain tissue seems to be the responsible cause Congenital anomalies are also possible factors

Other Complications Sclerosis of the renal and cerebral vessels may produce or increase an existing hypertension as pointed out earlier

Sclerosis of the splenic or hepatic arteries in this stage does not lead to complications A coexistent nephrosclerosis does not cause complications for

some time because an impairment of renal function can be found only by very sensitive special tests

Not rarely, diabetes appears in *this stage* and is attributed to a sclerosis of the pancreatic arteries *Glycosuria* is found frequently and should be looked for particularly after a meal rich in carbohydrates Nephrosclerosis however increases the renal threshold and may prevent glycosuria despite a markedly elevated blood sugar *The blood sugar level is therefore* much more important than the amount of urinary *sugar in* the appraisal of these cases

With rapid failure of the heart or following coronary thrombosis with myocardial infarction *or because* of slowly developing myocardial fibrosis the systolic blood pressure may *fall* while the diastolic remains at a high level Thus the pulse pressure *is reduced* markedly *In some* cases the diastolic blood pressure also falls to a normal level *then the* diagnosis of a former hypertension is suggested only by the discovery of an unusually large left ventricle We would like to stress again *the frequent* occurrence of fibrotic occlusion of secondary and tertiary branches *of* the coronary arteries in middle aged and elderly patients particularly *in the* presence of *hypertension* (Baurle Rau) This event receives too little consideration by clinicians

Renal Complications Only a small percentage of patients (7—10 per cent) reach the stage of *renal* insufficiency and die from uremia This event occurs most often in *the* group of patients who develop the syndrome of malignant hypertension

MALIGNANT HYPERTENSION

This is not *a disease* entity but rather a syndrome that appears in different diseases which *lead* to hypertension — essential hypertension chronic nephritis and pyelonephritis Therefore the term malignant phase or accelerated phase of hypertension *seems* to be more appropriate The pathogenesis is unknown but it seems to occur when the *diastolic* blood pressure is very high

Clinically the disease is said to have entered the malignant phase when the course is rapidly *downhill* when the diastolic blood pressure is elevated to values about 130 *mm* Hg and remains fixed at that level and the fundal changes (mentioned below) appear

Histologically the condition is characterized by the appearance of necrosis of the afferent *arterioles in the kidney* focal necrosis of the tufts a proliferative response of the glomeruli *and* diffuse endarteritis (proliferative capsulitis)

Malignant hypertension often appears in relatively young people In one series 67 per cent of patients were between 35 and 55 years of age one subject was only 17 (Ellis)

In principle the symptoms are those of essential hypertension but more accentuated *Headache* is common and progressive Papilledema and retinal hemorrhages are rarely *missed* The higher diastolic pressure causes a higher spinal fluid pressure leading to papilledema However Perera found papilledema when the *blood* pressure was low Renal function is impaired the specific

gravity becomes fixed and the blood contains an increase of nonprotein nitrogen and creatinine Albuminuria may be missed for some time but red blood cells appear in the urine early The differentiation from chronic nephritis is very difficult The outlook is always very bad and the disease runs a downhill course ending within a few years Death may occur within one year after symptoms appear

One of the best clinical signs is the elevation of the diastolic blood pressure to values above 130 even values of 160—180 are observed The marked narrowing of the arterioles responsible for this sign leads to renal insufficiency vascular wall necrosis and cerebral edema However the accelerated phase does not depend *on the height of the blood pressure (Perera) It may occur even when the blood* pressure is considerably lowered by cardiac accidents Palpation often shows a marked hypermotility of the heart as in hyperthyroidism and the whole precordium may pulsate The P R interval in the electrocardiogram is often shortened and unusual values of less than 12 hundredths of a second often are observed The serum of patients with renal insufficiency contains cardiotoxic substances which may be responsible (Raab)

The picture of malignant hypertension can be produced experimentally by the Goldblatt mechanism but not by neurogenic factors

In general the prognosis is very poor but spontaneous improvements do occur Fortunately improvement is more common with modern therapeutic measures The average survival time in the group observed by Schottstaedt and Sokolow was 8 5 months The two year mortality was reduced from 90 to 50 per cent by sympathectomy and currently is even lower with hexamethonium and apresoline The rice diet alone or any diet containing 20 grams of protein daily may abolish this syndrome and the azotemia may disappear with it Page found that therapy with pyrogens may be successful The patient receives bacterial pyrogens intravenously daily for one month so that the temperature is raised to about 38 Celsius after each injection

Prognosis

The prognosis of essential hypertension is difficult to ascertain since even a very mild form may suddenly assume a malignant course particularly in young people moreover complications like coronary thrombosis may appear unexpectedly and change the whole picture The mode of life the habits of the patient in regard to the quantity of food taken alcoholism and the like are important in the ultimate prognosis The prognosis also depends upon the sex of the patient women having in general a better prognosis

If patients have electrocardiographic changes indicative of myocardial damage and usually caused by coronary sclerosis or if gallop rhythm exists or if attacks of cardiac asthma have appeared the prognosis is dubious An elevation of the diastolic blood pressure above 120 mm Hg is significant — this may lead to progressive changes On the other hand patients may have a diastolic blood pressure of 130 mm Hg for years without developing evidence of the malig

nant phase Observations are on record in which a blood pressure of 220/190 was observed for 20 years or 225/140 for 16 years (Perera) and milder forms of hypertension for 50 years (Pratt) Women in particular sometimes tolerate excessive blood pressure well for many years The average duration of hypertension according to Perera is 19 years The height of the blood pressure is not the only factor important for the prognosis nor for the size of the heart or the changes in the electrocardiogram An improvement of the fundus or the disappearance of hypertrophy patterns in the electrocardiogram have been observed without change of blood pressure Burgess stressed the chances of a normal or nearly normal life expectancy in patients over 50 with hypertension in the absence of cardiac cerebral or renal damage

Therapy

In discussing the therapy of essential hypertension it is necessary to stress from the beginning that no rational therapy is available because we lack knowledge of the developmental mechanism of this condition Great progress has been made in symptomatic management however and therapeutic nihilism is unjustified

Five types of therapeutic measures will be discussed (1) general measures (2) diet (3) drugs (4) surgery and (5) symptomatic treatment

General Management The attitude of the physician when hypertension is found has primary importance Unfortunately too many physicians still frown and look very serious when they find a hypertension Advice is often given which convinces the patient that the situation is extremely grave Actually the patient must be told that the blood pressure is elevated, for without this information certain measures that require his cooperation are impossible On the other hand the exact readings need not be given despite the possibility that some patients will go from one physician to another until one is found who will unhesitatingly reveal the height of the blood pressure The patient attaches too much importance to the different levels of pressure found on different occasions a rise of 5 mm for example may mean impending disaster to him

After discovery of the hypertension it is advisable to do a general examination including (in advanced stages) tests of renal function (of which Volhard's concentration test or a modification thereof is still the most reliable) a roentgen examination of the chest an electrocardiogram and an intravenous pyelography If all these findings are negative it is important to stress that it is possible for the patient to live a symptom free active life and to live for a long time The hypertension need not cause complaints for 30 years It is important to stress that there is no danger of a stroke (the complication most dreaded by the patient) and that while there is need for continuous medical observation frequent visits are not required The patient should not become blood pressure conscious

A frank discussion of the mode of life should follow Sources of apprehension fear and anxiety should be abolished if possible Excessive mental strain should be avoided as well as physical overwork Excessive responsibilities extracurric

ular activities and emotional conflicts should be avoided If hypertension is discovered in young individuals a profession should be suggested in which mental and physical strain are minimal Rest periods vacations and long sleep at night should be secured The patient must avoid overeating The quantity of food is not less important than the quality The time is past when red meats or meat in general were forbidden Foodstuffs with a high content of fat such as eggs tongue liver cream and all fats are not permitted There is no proof that normal quantities of spices are harmful There is no objection to small quantities of alcohol in early phases but smoking should be forbidden since there are patients in whom the blood pressure always rises after smoking Sex problems must be discussed frankly and any undue excitement or apprehension in this question should be avoided Cystitis and *pyelitis* if present particularly in women must be treated by specific measures

The blood pressure may fall if obese people reduce their weight therefore a low caloric diet is warranted in such patients

Diet In recent years the diet in patients with hypertension has received increasing attention For years this was neglected and — in spite of the pioneer work of Allen in addition to that of Ambard Strauss and Volhard — was considered to be a peculiarity of Continental Medicine It is to the credit of Kempner that with the publication of his work on the rice diet the attention of physicians was again drawn to the importance of diet in hypertensive patients

At the present time one often sees as usual exaggerations of dietetic therapy Patients with a blood pressure of 150/100 mm Hg are put on a salt free diet and patients with coarctation of the aorta or old people with a purely systolic hypertension from atheroma and loss of elasticity of the ascending aorta are tortured by a strict salt free diet which of course is useless in such patients

A strictly salt free diet that is a diet containing not more than 200 mg of sodium leads to a fall of blood pressure in about 40 per cent of the patients Often it is not tolerated A salt poor diet containing around 500 mg of sodium only rarely helps The salt free diet is built on lanolac baked potatoes sugar and oleomargarine and is gradually amplified with the aid of diet prescriptions such as those made available by the American Heart Association In the first edition of this book we mentioned that the loss of sodium by the body is accelerated by a few injections of a mercurial diuretic but this measure is rarely necessary

RICE DIET On the basis of studies of the metabolism of isolated kidney cells Kempner introduced the rice diet initially only for renal hypertension guided by the idea that it would diminish the load on the kidneys just as the load on the heart is diminished in patients with cardiac damage by the avoidance of exertion Later the diet was employed in other forms of hypertension as well and with results that were startling

The diet consists of 250—300 grams of rice of any type daily with fruits and orange juice It contains about 2000 calories only 5 grams of fat 20 grams of protein daily 200 mg of chloride and 150 mg of sodium One banana daily is permitted avocados nuts and dates are avoided Fluids are given only in the form

of fruit juices and the amount should not exceed 1000 ml daily The rice is boiled or steamed the fruit and juices are fresh and canned ones are permitted only if no sodium salts were used to preserve them

Vitamin A (5000 U) Vitamin D (1000 U) thiamin chloride (5 mg) riboflavin (5 mg) and calcium pantothenate (2 mg) are given daily A little iron should be added After a few months some green (non leguminous) vegetables may be added and later lean meat broiled or boiled Weak coffee is also permissible

During treatment particularly in the first three weeks the serum sodium and urea should be watched because of the possibility of the patient losing large amounts of salt by the kidneys and developing hyponatremia and azotemia If mild azotemia is present it is not a contraindication to the diet

The diet is easy to explain but hard to follow It is monotonous and only a small percentage of patients have the will power to go through with it In those who do success with a considerable fall of blood pressure (in 70 per cent) and of cholesterol (in 40 per cent) will be accomplished The heart becomes markedly smaller the electrocardiogram becomes normalized and abnormal changes in the fundi disappear Headache and palpitation disappear Azotemia diminishes and the patient feels better

The method of action of this diet is not clear At first any effect was denied on the basis of brief observations of only a few patients Actually the diet must be followed for many months (for a year in one of our patients) until some effect is observed In others a fall of blood pressure is seen after four or five days Later investigations — by the Medical Research Council in Great Britain for example — yielded the same result that is a beneficial effect in 70 per cent Even in patients with papilledema astonishing results have been reported (Newborg and Kempner)

In spite of these results and the experiences of others one still finds remarks in the literature that the beneficial effect is obtained because of the fanaticism of the supervisors of the diet their influence on the psyche of the patient and similar effects But no fanaticism could abolish the papilledema of 23 out of 38 cases before the rice diet was introduced

The consensus at the present time apparently is that the diet s efficacy stems from its low content of sodium the chief argument being that patients who experience a fall of pressure during the diet show a rise as soon as salt is added We do not consider this a convincing argument since with other modes of therapy as well addition of salt may cause the pressure to rise The rice diet is poorer in fat and proteins than any other diet and the influence of these factors has had little study An action through the adrenals is one of the possibilities In the first three months the patient is in a negative nitrogen balance but soon particularly because of the protein sparing action of carbohydrates equilibrium is reached It has been stated that the rice diet should not be any better than one of barley or macaroni To this one must answer that rice is a staple food which contains more than any other the necessary amino acids only methionine and histidine are said to be lacking

It is astonishing that even on hot summer days the patients never develop a low salt syndrome provided salt does not leak from the kidneys Appearance of great lassitude headaches apathy anorexia and muscle spasm point to the presence of salt depletion

How long this diet can be continued without harm has not been established as yet

In patients who because of their occupation are not forced to eat in restaurants and who have the will power we consider the rice diet a measure that if followed certainly prolongs life

Here as in the salt free diet half measures are of no use Only strict adherence to the diet brings help It should not be abandoned before strict observance for a year has failed to bring about success

RESINS Resins will be discussed in further detail in the section on diuretics They are of help but are not a substitute for a salt poor diet In patients on a normal diet with reference to salt resins absorb only a small quantity With the use of resins certain risks are involved and the question of whether the slight increase of the salt intake possible with their employment helps sufficiently to take the risks and unpleasantness involved must be answered in the negative

In general the resins are disappointing in patients with hypertension In patients with hyperkalemia they may be useful in diminishing the potassium content of the serum and tissues

Drug Treatment Sedatives particularly phenobarbital and chloral hydrate with bromides have great value as an adjuvant to induce relaxation

Almost all of the drugs recommended during the years such as iodides preparations of garlic bismuth subnitrate and many others seem to be useless There is no proof that the frequently used purine derivatives have a beneficial effect We wish to reemphasize however that experimental atherosclerosis caused by cholesterol feeding can be prevented in rabbits by the simultaneous administration of iodine

SULPHOCYANATES Treatment with sodium or potassium sulphocyanate may have an appreciable effect in lowering blood pressure and in relieving headache Due to their great toxicity however these substances were soon abandoned although treatment involving their use has been revived repeatedly To reduce the incidence of toxic manifestations it has been recommended that the blood level of the thiocyanates be checked frequently

No explanation of the mechanism of the fall of the blood pressure during the administration of potassium thiocyanate is available An action through the adrenal cortex has been assumed

Administration of the drug is contraindicated in patients with kidney lesions because here even a single dose may elevate the blood level for 2 to 3 weeks Severe atherosclerosis cerebral complications congestive heart failure or angina pectoris are also considered contraindications

The single dose is 0 2 Gm The dose for different patients must vary because the individual excretion of the thiocyanates varies greatly Usually three tablets

of 0 2 Gm are given daily for three days and then two a day until a blood level of 8—12 mg per cent is reached The headaches disappear even with a level of 3—6 mg per cent With higher levels toxic manifestations are common They occur however even with lower levels Maintenance may be kept with one tablet a day or 3 to 5 tablets a week Continuous treatment for many months or years has been reported without complications or untoward signs On the other hand early toxic manifestations are frequent and develop in approximately 20 to 30 per cent of those treated fatalities have been reported despite biweekly determination of the blood level which never exceeded 10 mg per cent The plasma level may suddenly rise without apparent cause

The earliest signs of toxicity are weakness and nausea Dizziness hallucinations confusion and other psychotic manifestations with illusions depression convulsions and coma pains in the jaw thrombophlebitis purpura and dermatitis Cheyne Stokes breathing abdominal pain and fever may follow Signs of toxicity may persist for 3 or 4 weeks despite immediate cessation of treatment Often death is not preventable Therefore several observers oppose the general use of these dangerous drugs Our personal experience is in complete agreement with this attitude The blood pressure is appreciably reduced in about 30 to 40 per cent of the cases treated and symptoms such as headache may be greatly relieved But the dangers intrinsic to this method of treatment are great and no proof is available to show that it prolongs life The blood pressure rises soon after treatment is interrupted As with many other drugs the use of which yields occasional success but also dangerous complications many authorities are enthusiastic until they encounter the first fatality despite every precaution In rare cases however with an unusual rise of blood pressure and headache and the impossibility of giving relief by other methods potassium thiocyanate may be tried Its use in hypertensive crises was mentioned earlier It has been recommended (St Pierre) that sodium thiocyanate be injected intravenously in subjects with headache Twenty cubic centimeters of a solution containing I 396 Gm of sodium thiocyanate is injected This amount does not cause toxic blood levels

Since therapy with thiocyanates diminished the blood pressure decidedly in some cases the question arises whether this reduction is not associated with danger As soon as organic changes develop in the arterioles it is argued hypertension is a necessary compensatory mechanism to insure tissue nutrition If the blood pressure falls less blood is forced through the narrowed vessels into the tissues and their nutrition suffers Urea clearance tests however reveal no diminution of kidney efficiency in hypertensives following marked reduction of blood pressure with thiocyanates On the other hand it is a common observation that a slight reduction of blood pressure following coronary occlusion may be associated with evidence of disturbed cerebral blood supply or an increase of blood nonprotein nitrogen and creatinine these signs promptly disappear when the blood pressure rises again

RAUWOLFIA SERPENTINA This climbing shrub from the foothills of the Himalayas and the Malayan peninsula was known for centuries in India as a

remedy for hysteria some forms of insanity for snake bite and as a vermifuge In recent years Indian physicians first became aware of the beneficial effects observed when this drug was used in hypertensives The crude extract from the root leaves or a purified fraction (alseroxylon) of the plant or a purified alkaloid (reserpine) are used Actually a fall of the blood pressure occurred according to one observer in 60 per cent of patients treated A good effect is obtained from this tranquilizing agent particularly in nervous irritable patients with mild hypertension but remarkable improvement was also observed in malignant hypertension In those patients in whom Rauwolfia preparations do not help the administration of veratrine or Apresoline in addition often brings improvement In rare cases there was an orthostatic hypotension without collapse The blood pressure begins to fall in some individuals after 3 to 12 weeks Following intravenous injections there is a latent period of an hour While originally larger doses were used the Food and Drug Administration now recommends that only the equivalent of 0 25 mg of Serpasil or rescinnamine be administered daily Larger doses may depress the blood pressure more but the side effects increase too much The hypotensive effect may persist after the drug has been discontinued for four weeks

The relative harmlessness of reserpine is illustrated by the following episode a 20 month old boy ingested 260 mg of reserpine (Serpasil) He slept during most of the succeeding twenty four hours his face was flushed and the temperature was 101 4 F There was a tachycardia The sleep was not deep and the child could be awakened at any time for feedings There were no after effects

In patients with rheumatic valvular lesions or coronary sclerosis on the verge of decompensation the appearance of severe edema and hepatic enlargement is noted when Rauwolfia preparations are given

Some of the side effects — which are few — are useful One is bradycardia or at least a reduction of the pulse rate by 10 per cent This seems to be caused by a central inhibition of sympathetic tone Another is the disappearance of constipation Loose bowel movements slight light headedness diminished libido at the beginning of therapy muscle and joint pains bronchitis stuffiness of the nose rarely epistaxis or bloody discharge otitis restlessness anxiety nightmares gain in weight fatigue buzzing in the ears and even Horner s syndrome are observed Diminished activity leads to gain in weight No tolerance develops and the therapy can be continued for years

A more serious and not extremely rare complication especially when larger doses are used is marked mental depression Some authors found mental depression in 10 per cent of their patients treated with the alkaloid reserpine Some report a similar effect on the blood pressure but no mental depression when another alkaloid — rescinnamine — was used The mental depression particularly occurs in patients with depressive tendencies or maladjustment earlier in their lives After cessation of the drug the depression may persist for 4 to 6 weeks Suicidal tendencies agitation and insomnia occur particularly with larger doses

Parkinsonism appears often if larger doses are used Epistaxis diminished mental activity inability to concentrate and impaired judgment have been reported Exacerbation of ulcerative colitis occurs It is still undecided whether peptic ulcer is a contraindication Hemorrhages are observed during medication Gastric hypersecretion is common

It seems that there is a greater fall of the diastolic pressure with the administration of preparations made from the crude root than with reserpine The differences are however small The Rauwolfia alkaloid rescinnamine is as effective as the alkaloid reserpine It causes the same side effects however often with less severity There are patients who exhibit with reserpine on the other hand a lesser degree of some side effects than rescinnamine

Achor et al found nasal stuffiness in 83 per cent of their patients dreaming or nightmares in 42 per cent depressive effects in 17 per cent laxative effects in 28 per cent muscle aches or cramps in 9 per cent dizziness in 6 per cent and urinary urgency in 4 per cent It has been recommended to omit the drug in one week of four when very marked untoward effects appear Since administration of only 0 5 mg of reserpine for two weeks often caused massive gastric hemorrhage or perforation of a gastric ulcer it has been recommended not to give larger doses than 0 25 mg daily Great caution is also indicated in persons with a history of ulcerative colitis

In patients on Rauwolfia therapy undergoing surgery significant hypotension marked bradycardia have been observed during the anesthesia It has therefore been recommended that treatment with these drugs be omitted at least 2 weeks before elective surgery (Coakley et al)

Rauwolfia preparations have the advantage of normalizing the blood pressure and not causing subnormal pressures Many patients experience a pleasant sensation of calmness and well being during the use of these compounds while an exceptional patient must stop using them because of unpleasant side effects particularly increased excitability

The mode of action is for the most part central (hypothalamic) but stuffiness of the nose and other observations point to an action on the autonomic nervous system Interaction between reserpine and serotonin has been reported (Shore et al) Reserpine increases the discharge of metabolites of serotonin which act as antiserotonins It is said to antagonize the blood pressure rise due to serotonin under certain experimental conditions (Schneider and Pinehart) or to displace serotonin in the central nervous system

In most cases 0 25 mg of reserpine daily or 100 mg of the root extract daily suffice Combination of Rauwolfia with chlorpromazine (Thorazine) has been recommended Of the latter drug 15 mg was given three times a day (Fiber) Reserpine given intramuscularly in the amount of 2 5 mg causes a marked predictable hypotensive effect which begins after 3 hours The fall of the blood pressure is smooth In crises 2 5 mg are injected every 12 hours

HYDRALAZINE (APRESOLINE) This phthalazine derivative has a chemical structure that is new in therapy (Bein et al) It is remarkable because it brings

about a fall of blood pressure in 60 per cent of patients but side reactions are seen with relatively small doses in about 70 per cent of those treated Johnson and associates saw the blood pressure fall to normal limits in 42 per cent of their patients It was lowered in an additional 23 per cent Despite the fall of blood pressure the blood flow through the kidneys is increased There is a tachycardia apparently caused by direct stimulation of the heart

The side effects consist of headaches flushing peripheral edema hemorrhages in the gastrointestinal tract palpitation giddiness anorexia hiccups a grippelike syndrome with fever anginal pain (the drug is contraindicated in coronary sclerosis but how can one be sure of its absence?) nasal congestion lacrimation tachycardia skin rashes periorbital edema drowsiness or over stimulation myalgia pancytopenia tingling of the extremities nausea and vomiting

When large doses are given for a while (over 600—800 mg) rheumatoid arthritis and syndromes like those of the collagen diseases appear occasionally a picture similar to the one of lupus erythematosus is observed even with L E cells in the blood There is a rash fever arthritis anemia hematuria an enlargement of spleen and lymph nodes One observer saw this syndrome in 13 out of 139 patients who were treated with doses over 800 mg daily Lee found the lupus erythematosus syndrome in 12 per cent of the patients receiving more than 300 mg of hydralazine daily

One begins with doses of 20 mg four times a day by mouth and gradually raises this amount after 4 to 6 days until a desired effect is obtained or some of the numerous side effects force discontinuance of the therapy Some side effects disappear when an antihistaminic drug and aspirin are given with every dose of hydralazine Many side effects disappear with continued treatment Following an intravenous injection of 2 5 mg the blood pressure falls within a few minutes and returns to the original level after 4 to 8 hours

In many cases another drug capable of lowering blood pressure must be added to obtain success Some patients develop tolerance In some daily doses of even 900 mg have no useful effect

The mode of action of the drug is not established and seems to be complex There is certainly a depressant effect on the vasopressor center and a slight sympathicolytic and adrenolytic action The chief effect is relaxation of smooth muscles Some of the pressor substances (pherentasin) circulating in the blood are inhibited

In hypertensive crises an intravenous injection of 20—40 mg causes a fall of blood pressure for several hours

ERGOT PREPARATIONS Ergotamine tartrate and dihydroergotamine 45 have a peripheral vasoconstrictive action The three compounds dihydroergocrystine dihydroergokryptine and dihydroergocornine given in equal parts (manufactured under the name of Hydergine) lower the blood pressure In acute rises of blood pressure the amount of 0 3 mg given intravenously after dilution with saline causes an appreciable fall of blood pressure but the oral adminis

tration of this adrenergic blocking agent is disappointing although favorable reports have appeared in the literature Mild effects are counterbalanced by resistance which appears early Nasal stuffiness and bradycardia are noted

DIBENAMINE AND RELATED COMPOUNDS Dibenamine belongs to the alkyl amines and is a peripherally acting adrenergic blocking agent It causes severe toxic effects and cannot be given orally it was soon abandoned The slightly modified but similar compound Dibenzyline is given in doses of 20 mg in the form of gelatin capsules Its side effects are gastrointestinal irritation syncope on standing drowsiness nasal stuffiness and weakness Because these side effects exist it is rarely recommended

Priscoline an imidazoline may cause marked rise of blood pressure angina pectoris exacerbation of a peptic ulcer and has been abandoned for the treatment of essential hypertension

VERATRINES Veratrine has been used for almost a century in eclamptic toxemia of pregnancy and hypertensive encephalopathy In recent years some of the alkaloids have been isolated particularly protoveratrine which has the advantage that the dose is regulated according to the weight and not by bioassay

Veratrines (Veriloid for instance in the form of tablets containing 2 or 3 mg each is given 3 to 8 times daily) cause a fall of blood pressure via the Bezold Jarisch reflex that is increasing the centripetal stimuli from cardiac receptors and carotid sinus receptors via vagal nerves leading to lowering of the vasoconstrictor tonus Other preparations are Unitensen and Vergitryl A pronounced bradycardia accompanies the fall of blood pressure If excessive atropine abolishes it Provell maleate or Veralba are purified protoveratrine preparations which can be obtained as tablets of 0.2—0.5 mg Up to 6 mg have been given daily Initially one gives 0.5 mg three times daily

Hoobler et al advise giving 0.50 to 1.5 mg after breakfast orally A dose of 0.25 mg is given at 10 a m and the same dose is repeated after lunch

In acute emergencies (hypertensive crises) protoveratrine has been given intravenously (1.5—1.9 micrograms per kilogram) slowly over a two minute period and later 20 micrograms every ten minutes until an effect is obtained Orally subcutaneously and intramuscularly doses of 0.5—0.75 mg four times a day have been used The substance acts within 30 minutes for 1 to 3 hours In general the individual dose varies so much that with all veratrine preparations the trial and error method must be used Thus one begins with the doses mentioned and gradually increases them The disadvantage of therapy with veratrine lies mostly in the fact that effective doses usually cause gastrointestinal symptoms i e nausea and vomiting The nausea appears in some individuals even with the smallest doses

Other side effects consist of substernal and epigastric oppression lethargy and giddiness palpitation salivation and rhinorrhoea Postural hypotension is usually not observed

METHONIUM COMPOUNDS Penta and hexamethonium are quaternary ammonium compounds with a curare like action and are therefore autonomic

ganglion blocking agents Hexamethonium salts are stronger and hexamethonium chloride is preferred to the bromides and iodides owing to the side effects of these ions The ganglion blocking effect is similar to that of tetraethylammonium chloride which also has been recommended but which has been abandoned Most of the effects caused by blocking sympathetic ganglia are useful because peripheral arteriolar resistance is reduced while blockade of the parasympathetic ganglia causes unpleasant side effects

Hexamethonium is a very potent drug which initially should be given only in a hospital with constant supervision The patient should be informed about its side effects (which are mentioned below) in order that he may obtain help in time and avoid apprehension

With oral administration only about 5 per cent of the hexamethonium administered is absorbed by many individuals and therefore the effect is not satisfactory in the majority of patients unless large doses at least 125 mg are given four times a day at the beginning This dose is increased every 5 or 6 days until the desired effects are obtained Not more than 5 grams are given daily For intravenous administration we recommend not more than 2 5 mg as the first dose since we observed precipitous fall of the blood pressure with the usually recommended amount of 5 mg Patients who are on a salt free diet and those who have had a sympathectomy respond with special speed The doses are varied as necessary according to the response of the patient and must be increased after a while since tolerance is very common and a great handicap In the progress of therapy sometimes the ultimate dose has been ten times as large as the initial and very effective ones The intravenous injection acts within a minute the intramuscular within 5 to 15 minutes and the hypodermic within 30 minutes The effect following subcutaneous injection is maximal after one hour Three to 6 injections a day are given

Success is obtained in about 60 per cent of the patients

The therapy is contraindicated in patients with azotemia glaucoma marked prostatic hypertrophy severe cerebral and coronary sclerosis severe constipation and marked renal damage

Because the autonomic ganglia are blocked to a different degree the side effects vary considerably in different patients Some of the effects deserve careful attention by the physician and require special therapy

One of the first side effects is constipation The patient should not go for more than 48 hours without a bowel movement Paralytic ileus has been reported During constipation larger amount of the compound are absorbed One gives milk of magnesia at the beginning and cascara later the action of hexamethonium on vagal ganglia is counteracted by compounds like urecholine (urethan or beta methylcholine) given in doses of 5—20 mg daily It is not always effective Five milligrams of pilocarpine nitrate or 15 milligrams of prostigmine bromide 1 to 3 times daily may help

Another great danger is urinary retention which is at times very annoying Complete and irreversible sympathetic paralysis with hypotension has been

observed fortunately it is only rarely that it cannot be corrected with neosynephrine or other pressor amines Disappearance of libido and diminished potency is observed but omission of one dose of the compound often corrects this Because of the curare like action general muscular weakness is often noted One of the most common side effects is the orthostatic hypotension which is seen with this compound more than with any other It appears particularly after a heavy meal consumption of alcohol and in hot weather (the patients cannot sweat) Often the blood pressure in the supine position must be kept at a higher level than desirable in order to avoid marked fall when the patient is erect Blurring of vision due to paresis of accommodation is common Interstitial pneumonia has been seen particularly in azotemia (Golden and Bronk) Pulmonary edema and fibrosis develop causing death from asphyxiation (Viersma) Some patients complain of dryness of the mouth due to decreased salivation Otitis media may be seen because of dryness of the Eustachian tube A greater incidence of dissecting aneurysm in hypertensives treated with methonium or pentolinium has been reported

As with Rauwolfia congestive cardiac failure may develop Permanent bilateral blindness following a fall of blood pressure from 246/136 to 180/110 mm Hg in a 34 year old woman has been described (Bruce)

Because of the danger of severe orthostatic hypotension it is important to determine the blood pressure with the patient standing

PENTAPYRROLIDINE (PENTOLINIUM TARTRATE) Pentolinium (Ansolysen) is a synthetic ganglion blocking agent which is apparently superior to hexamethonium and has replaced it It has been estimated to be about five times as strong as hexamethonium and the average duration of its action is longer This claim has been denied by others It is alleged that its action is less variable and the dose necessary to elicit an effect varied between 135—630 mg a day (Freis et al) Some patients need more than 1000 mg per day Side effects are claimed to be less common than with hexamethonium but are the same in nature and strict supervision of the patient especially in regard to the blood pressure in the erect position and bowel movements is equally necessary Heart failure with retention of salt and water caused by therapy with pentapyrrolidine has been described

One gives 10 mg three times a day (every 8 hours) starting one hour before breakfast The dose is increased by 10 mg every second day until dizziness appears in the erect posture The ideal dose is about 20 mg less than that which produces vertigo and fainting The maximal effect appears one to one and a half hours after the administration and lasts for 6 to 8 hours Some authors recommend giving twice the single daytime dose just before bedtime If hypodermic injections are employed one starts with 3 mg three times a day (every 8 hours) The amount is increased if necessary by 0 5 mg every second day

All these ganglion blocking agents are administered at first in the hospital for 3 weeks For the first 5 days it is best to take the standing blood pressure every 20 minutes after each dose omitting only night tests

Heavy meals and alcohol influence absorption An ideal blood pressure is 120 mm Hg systolic this is easily accomplished in the erect patient

Ecolid (chlorisondiamine) is another ganglion blocking agent effective orally and requiring smaller doses It has a longer action than hexamethonium The orthostatic blood pressure must be checked In the study of Grimson the average effective dose varied between 50—100 mg given twice a day This is recommended because of the long action of the drug (12 to 20 hours) One begins with 25 mg per dose Blurring of vision is often disturbing

Inversine hydrochloride (*mecamylamine*) is considered superior as a ganglion blocking agent because it is completely absorbed after oral administration and acts for 6 to 36 hours Inversine is not a quaternary ammonium compound like the other ganglion blocking substances but a secondary amine

One gives initially 2 5 mg once or twice daily by mouth This dose is increased by 2 5 mg every second day until the necessary dose is reached Side effects are very common Seven out of 35 patients who were treated with this substance showed an unusual neuromuscular disorder with tremor anxiety and convulsions (Schneckloth et al) The average dose to which patients respond with a significant fall of blood pressure is 25 to 30 mg Like other similar agents it is given at first only to cooperating patients in hospitals The side effects and dangers are the same as with hexamethonium Psychoses were observed

COMBINATION THERAPY WITH HEXAMETHONIUM AND HYDRALAZINE This method (Hyphex therapy) warmly recommended by Schroeder is said to reduce the blood pressure to normal values in almost 100 per cent of the patients

In the following paragraphs we shall follow the rules elaborated by Schroeder In view of the side effects sometimes dangerous and sometimes very annoying treatment with these two compounds should be started only in a hospital where the patient is ob erved for at least three weeks Treatment is never started with both drugs simultaneously One should be aware that in severe coronary stenosis with angina pectoris a fall of blood pressure may induce a myocardial infarction Renal function should be satisfactory (phenol red test) Even an encephalogram should be done to rule out a dysrhythmia which with a decided fall of blood pressure may change to a cerebral accident

With the patient seated the blood pressure is taken every four hours day and night

On the first day one starts with the administration of 125 mg of hexamethonium every four hours by mouth If the blood pressure falls to values below 150 mm Hg a dose is omitted Care is taken to ensure bowel movements by means of milk of magnesia or cascara On the second day 250 mg of hexamethonium are given in tablet form every 4 hours with the same precautions and on the third day 375 mg at the same intervals On the fourth the dose is increased to 500 mg every four hours always omitting the dose if the blood pressure falls to below 150 On the fifth day for the first time Apresoline (hydralazine) is given in addition using 25 mg every four hours by mouth On the sixth day the amount of Apresoline is doubled the amount of hexamethonium remaining

the same On the seventh day the dose of Apresoline is increased to 75 mg every four hours By this time the patient usually has side effects and must be persuaded to continue the treatment On the eighth day 100 mg of Apresoline are added to the hexamethonium every four hours If low pressure is attained on one of the preceding days the doses are not increased

It is claimed that with this method a reduction of the blood pressure to normal levels is accomplished in almost every patient After prolonged therapy after the diastolic blood pressure becomes normal the dosage of these drugs can often be diminished (Perry and Schroeder) The same authors had remarkable success in the therapy of malignant hypertension with renal azotemia with the use of ganglionic blockade combined with hydralazine of 46 patients with a nonprotein nitrogen of 30—60 mg per cent 27 were alive and working after almost two years

The effects of the compounds and the accidents caused by the reduction of blood pressure are the same as mentioned above

SUGGESTIONS ON DRUG MANAGEMENT OF HYPERTENSIVES At the present time it is recommended that all patients with hypertension except those with an excessively high systolic blood pressure and with a diastolic above 120 mm Hg be started with Rauwolfia therapy If this method does not bring success within two months we suggest the addition of veratrine or hydralazine For this purpose the mixtures of the latter two drugs which are prepared by the manufacturers are not used Rather veratrine or hydralazine are given in increasing individual amounts ready made tablets do not permit individualization of the treatment

Ganglion blocking agents are necessary only in excessively high systolic and diastolic blood pressures If possible one starts with a Rauwolfia preparation here also and adds Inversin in increasing amounts This is preferable since Rauwolfia in combination with other drugs shows not only an additive but also a synergetic action

A salt poor diet is advised A salt free diet is not recommended since it can rarely be maintained for several years and is of help only in some patients The treatment with the modern drugs makes this impalatable diet unnecessary If the patient who comes for advice already is on a salt free diet there is no reason to tell him to discontinue it

Surgical Therapy At first performed by Pieri for the treatment of hypertension sympathectomy was developed interestingly enough at a time when knowledge of the renal factor in the genesis of hypertension was in the process of investigation and when many clinicians thought that the Goldblatt mechanism was an adequate explanation of the pathogenesis of essential hypertension There is general agreement that the experimental renal hypertension is humoral and is uninfluenced by sympathectomy

The methods of sympathectomy devised are diverse but one fact gradually emerges operations with most extensive severing of the sympathetic system provide the greatest chance for success

A report of 350 cases in which a *supradiaphragmatic* sympathectomy was done (Peet et al) revealed a significant reduction of blood pressure in 51 4 per cent and a relief of major symptoms in 86 1 per cent

With a *subdiaphragmatic* extraperitoneal sympathectomy with resection of the splanchnic nerves a part of the coeliac ganglion and the upper lumbar sympathetic trunk (Allen and Adson) 13 per cent of 224 postoperative cases responded well and 18 per cent to a fair extent In 39 per cent the fall of blood pressure was only temporary and the operative result was poor in 30 per cent There was no mortality

With the *combined approach* that is lumbo dorsal sympathectomy the operation is performed on one side and after about 10 days on the other side Recently both sides have been operated on simultaneously (Smithwick) The sympathetic trunk from the ninth dorsal to the second lumbar ganglion is removed and the great splanchnic nerves are severed

At present sympathectomy is considered to be indicated when the course is progressively downhill when the patient develops papilledema despite medical therapy when the diastolic blood pressure rises to values above 130 in spite of all medical measures when such measures do *not* improve very severe headache and when the mode of living of the patient or his occupation make adherence to the diet or medical therapy under supervision impossible

The operation is not performed in patients beyond 55 or 60 with renal insufficiency (urine concentration not over 1 010 or NPN not below 40) cardiac failure not improved by therapy or very advanced coronary or cerebral vascular sclerosis One should not operate in the presence of an active peptic ulcer

The mortality is 1 to 3 per cent Complications are atelectasis pleural effusion pneumothorax and disturbed ejaculation Operation on a pregnant woman did not prevent normal termination of pregnancy Hospitalization for 4 to 6 weeks is necessary but is appreciably shorter when both sides are operated on at the same session

The prognosis and results of the operation seem better in females With more extensive sympathectomy postural hypotension develops and may persist for weeks and even months The resultant disability is of variable intensity Anhidrosis of the lower extremities develops and ejaculation is lost if the second lumbar ganglion is removed In spite of all these difficulties and handicaps surgical therapy has more to offer in certain patients than any medical measure now available

For the postoperative orthostatic hypotension it is necessary to bandage the legs

The mode of action of the operation is not clear The pooling of blood in the lower part of the body in the erect posture is one of the possible reasons for the fall of blood pressure The operation does not and cannot bring about a cure it can only improve the condition

It is impossible by means of any test to predict the result of the operation in advance In mild cases the success may be meager in advanced cases even

in malignant hypertension the success may be astonishing Unfortunately in many patients the success is only temporary and after a while the blood pressure rises again

Among 275 postoperative patients in the literature Gerbaux noted a very good result in 25 per cent and only moderate improvement in 15 per cent In 28 9 per cent Ray found a normal or almost normal blood pressure postoperatively and in a further 31 6 per cent a significant reduction There was complete failure in 10 per cent According to others good results were seen in 21 per cent but they persisted only in 10 per cent The life expectancy is increased according to Hammarstroem Others have found no change in the lighter milder cases The survival time was increased only in very sick patients Similar results were obtained by Longland and Gibb but better ones by Zintel et al Many of the contradictory results stem from the fact that different methods were employed in selecting patients for operation

A precipitous fall of blood pressure may lead to the appearance of anginal pain and intermittent claudication

UNILATERAL KIDNEY DISEASE The question whether the hypertension disappears following removal of the diseased kidney in unilateral kidney disease has been much debated Since this is not the case in some instances some authors deny the possibility of any cure of hypertension by such a procedure There are however an increasing number of reports in which blood pressure fell when the diseased kidney was removed and particularly in children with hypertension resulting from unilateral pyelonephritis the elevated blood pressure returns to normal following operation (Gasul) In some cases — as in experiments — secondary changes in the other kidney and the entire vascular system preclude a fall of blood pressure even if the obviously damaged kidney is removed

ADRENALECTOMY The newest surgical procedure is adrenalectomy first recommended by Crile and later employed by Wolferth and Thorn and their associates This operation is logical because much work proves the necessity of the adrenals for the maintenance of various forms of experimental hypertension In man if adrenal insufficiency develops hypertension if present disappears and hypotension develops Experimental hypertension does not appear when adrenalectomy has been performed previously Adrenalectomy in man became possible since the adrenocortical hormones became available Thorn et al removed both adrenals completely Wolferth et al reported subtotal adrenalectomy with and without splanchnicectomy Patients should be under 50 years of age without azotemia and without advanced cardiac damage or encephalopathy When cortisone therapy is interrupted patients collapse within 24 to 48 hours In extremely hot weather under various conditions of stress the dose of cortisone (3—60 mg daily) which is often astonishingly small must be increased Sudden death occurs after the operation Even total adrenalectomy does not bring success in some patients! While it is too early to state definitely whether the operation should be performed more often it is certain that it allows many

patients with advanced malignant hypertension to survive and they may recover from a very critical situation

Adrenalectomy is done in uncontrollable hypertension without renal damage when without the operation death can soon be expected Usually the operation is performed in two stages

The measure is still in an experimental stage

Symptomatic Therapy The treatment of the individual symptoms of essential hypertension does not require detailed discussion Cardiac decompensation and angina pectoris are treated in the usual manner If vascular crisis and encephalopathy appear the administration of chloral hydrate and the intravenous injection of hypertonic glucose solution and of magnesium sulfate (20 cc of a 10 per cent solution slowly injected) has been recommended An intravenous injection of protoveratrin is given as rapidly as possible We prefer this compound to Serpasil or hexamethonium

In cerebral vascular accidents the least possible treatment is the most satisfactory one Morphine should be avoided in order not to depress the respiratory centers and not to raise the spinal fluid pressure The value of stellate ganglion block is still under discussion Venesection has the disadvantage of being followed by an additional rise of blood pressure Magnesium sulfate is given for convulsions and cerebral edema

Massage as well as passive and active movement should start early

Despite remarkable results in some cases — the disappearance of papilledema in the malignant syndrome normalization of the blood pressure in a long established hypertension through the rice diet or sympathectomy — there are still those who claim that the game is not worth the candle (Leonard) It is true that often no relief or improvement can be effected as a matter of fact the above mentioned measures have the effect of calling the patient s attention every day to his blood pressure thus making his life truly miserable On the other hand do not patients with diabetes also have to be constantly aware of their illness? And is the result not worth the disadvantages? If future statistics show that treatment initiated sufficiently early stops the further development of the illness that life is prolonged and that complications develop more rarely then a great victory will have been won in the battle against a condition the best advice for which in the past was Take is easy and swallow some phenobarbital

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Chapter 21

Hypotension

No GENERAL AGREEMENT has been reached regarding the level of the blood pressure at which hypotension may be diagnosed Most observers concur that a systolic blood pressure of 100 mm Hg or less permits the diagnosis of hypotension but some place the upper level at 110

In the new born the systolic blood pressure varies between 50 and 60 mm Hg It gradually rises to values just under 100 mm Hg in children up to the tenth year At puberty the normal blood pressure level for the individuals is reached At this period of life temporary periods of mild hypertension are observed they seem to be caused by an endocrine imbalance

One may distinguish between (1) symptomatic hypotension (2) constitutional permanent hypotension and (3) orthostatic hypotension

Symptomatic Hypotension

This is encountered in the course of various diseases It is common in Addison s disease and in Simmond s hypophyseal cachexia It occurs in shock collapse and during many infectious diseases Hypotension is a common sign of myocardial infarction Pulmonary emphysema bronchial asthma and pulmonary tuberculosis are often associated with a low blood pressure Various forms of neurogenic and hormonal hypotension are discussed by Raab

Permanent Constitutional Hypotension

Incidence This condition was formerly known as essential hypotension and is a common phenomenon It appears in about 3 per cent of otherwise healthy adults Like hypertension it is often familial

Symptoms In a vast number of cases the condition is devoid of symptoms and its discovery is accidental In this instance the physician errs grievously if he informs the patient about the finding Laymen are soon convinced that a serious disease is present and many patients date the beginning of their complaints to the time they were told their blood pressure was too low As a matter of fact this type of hypotension never leads to alarming symptoms it is an anomaly rather than a disease

The associated symptoms are increased lassitude fatiguability palpitation cold clammy hands and feet inability to concentrate and giddiness particularly on any change of posture Patients may suffer from headache and they always

feel chilly The responsibility for all these symptoms in a given case is hard to establish The condition is more common in females than in males

Prognosis The prognosis is excellent Statistics show that the mortality of these individuals is far below that of the general population and the history often reveals longevity in many members of the patient s family

Treatment As a rule medical therapy can be omitted It usually suffices to inform the patient about the nature of his condition its harmlessness and excellent prognosis Physical exercises massage sponge baths followed by brisk rubbing the application of an abdominal support for patients with enteroptosis and the administration of sedatives for the irritable nervous individual are often helpful A gain in weight is beneficial for these patients but this is extremely difficult to achieve in many instances

It is a mistake to administer drugs in order to elevate the blood pressure Ephedrine paredrine sympathol and adrenocortical extracts have been recommended and are still prescribed too often With these drugs it is impossible to maintain the blood pressure at a higher level for decades and furthermore this is entirely unnecessary If the patient can learn not to focus attention on the level of the blood pressure the symptoms soon disappear in most cases

Orthostatic Hypotension

In the third group low blood pressure appears transiently on changing from the horizontal to the erect position

Unless certain reflexes were active such change of position always would immediately be followed by syncope In the erect position the vascular bed of the lower part of the body is dilated by increased hydrostatic pressure and plasma is lost by increased filtration pressure Cerebral anemia so called orthostatic arterial anemia would appear if certain vasoconstrictive reflexes and an increased heart rate did not act as compensatory and adaptive factors

Therefore under normal conditions when the individual changes from the recumbent to the erect position only minor changes of blood pressure occur The systolic blood pressure falls slightly the diastolic rises a little and the heart beats a little faster

After prolonged recumbency in patients with varicose veins in tabes and in women in the first month of pregnancy this orthostatic hypotension with fainting occurs

In young and healthy individuals vigorous exercise may lead to orthostatic hypotension and even syncope because of pooling of blood in the lower extremities

In normal subjects under great nervous tension a temporary 0 diastolic pressure has been observed in the brachial artery while it was normal in the popliteal artery There is usually a tachycardia The phenomenon may last from a few minutes up to an hour and a half

As will be shown in the next chapter the normal adaptive mechanisms are greatly disturbed at times in such a way as to produce syncope when the posture is changed

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Chapter 22

Fainting; Morgagni-Stokes-Adams Attacks

Fainting

Introduction

The functions of the central nervous system and the preservation of consciousness depend upon an adequate blood supply. Accordingly, attacks of syncope are a natural consequence of certain disorders of circulation.

The laity frequently attributes syncopal attacks, whether accompanied by convulsions or not, to organic heart disease. As a matter of fact, fainting and convulsions are more common in cardiac patients than in the general population. Many patients with these symptoms do not, however, suffer from any circulatory disorder.

Formerly, "fits" (syncope with convulsions) were sharply distinguished from syncope (simple fainting). The latter was considered to lack an aura, to appear only when the patient was erect, and to display no motor phenomena, such as twitching or convulsions. At present it is generally agreed that the two conditions merge imperceptibly and the appearance of one or the other is determined only by the degree and duration of the circulatory disturbance.

Syncope accompanied or unaccompanied by convulsions is frequently confused with epilepsy. Mistakes also occur in the other direction, since epilepsy (petit mal) may manifest itself by simple syncope. Some of the circulatory disturbances discussed below may be preceded by an aura and may be accompanied by tonic clonic convulsions and loss of sphincter control. Possible confusion is enhanced by the fact that patients whose attacks originate in circulatory disturbances may present normal findings if a routine examination is done in the interval between attacks. Therefore, it is not astonishing that many patients who suffer from syncope of circulatory origin are referred by the neurologist, sometimes only after considerable delay. The confusion has found expression in the term "épilepsie cardiaque," which often appears in French literature.

Some types of syncopal attacks — fainting spells of patients with mitral stenosis, especially in those with a ball thrombus in the left atrium, and the fainting observed in patients with aortic stenosis or high pressure in the lesser circuit — were mentioned in previous chapters. The overwhelming agony in coronary occlusion and in aortic dissection may cause syncope. Unconsciousness appears in aortic dissection when it occludes the orifice of the innominate artery

and the left carotid artery Attacks of syncope due to a congenital anomaly of the carotid artery have been described (de Meyer Smith and Hinshaw) Fainting caused by thrombosis of the internal carotid artery or in pulseless disease will be discussed in the chapter on peripheral vascular disease

Vaso Vagal Syncope

Attacks of unconsciousness can occur in patients without circulatory or cardiac disease merely from sudden excitement and emotions Some patients (mostly women) faint whenever they see a funeral procession or at the sight of an open wound or blood An overcrowded or overheated room may cause fainting in others The sight of instruments may make the patient faint in the dentist s office others swoon upon receiving news of vital importance or on witnessing an accident Anxiety fear and pain are responsible

The attacks are particularly prone to occur on recovery from an acute infectious disease and in the course of an acute gastroenteritis They are not unusual in the menstrual period The syndrome is also encountered fairly often in tall rapidly growing individuals especially when they are compelled to stand quiet for a while Occasionally they may even occur when the patient is seated or lying

Pallor appears quickly the patient experiences great weakness and an unpleasant sensation in the epigastrium yawning is common At first the pulse is rapid and almost imperceptible The blood pressure may fall to below 80 mm Hg The patient may be drenched with perspiration On recovery a marked bradycardia sets in which may reach 30 beats per minute or less This bradycardia led to the introduction of the term vaso vagal syncope ' (Lewis) but this expression should not be confused with the vaso vagal attacks described by Gowers In the latter the patients (also for the most part women) do not lose consciousness but are overwhelmed by an inexplicable fear of impending death In the vaso vagal attacks sighing as well as yawning are common and nausea with vomiting are frequently noted Great weakness and headache may persist for hours Some uncertainty or dizziness are premonitory signs The attacks may last for seconds or minutes During the periods of unconsciousness spasmodic movements of the head and arms occur

The mechanism of these attacks is not adequately explained The suggestion that they are of vagal origin (Cotton and Lewis) or are due to abnormal carotid sinus reflexes (Lewis) is not fully substantiated The bradycardia and hypotension seem to develop *after* the onset of unconsciousness and are therefore not initiating factors

The syndrome consisting of the unconsciousness with nausea profuse sweating and bradycardia but otherwise normal findings is readily recognized

Complete assurance of the patient is entirely justified The condition is embarrassing but harmless

Postural Hypotension

This syndrome has special features (Bradbury and Eggleston) and therefore is separated from orthostatic hypotension The systolic and diastolic blood pressure in patients with this disturbance rapidly fall to low levels when the erect position is adopted The attacks are also apt to occur with the beginning of slight exertion such as walking on level ground when the lower part of the body receives more blood

Whereas symptoms usually occur in other types of hypotension when the systolic blood pressure declines to 80 or 90 mm Hg on change of position in this syndrome the systolic blood pressure may fall to 50 mm Hg without the appearance of symptoms There is no nausea sweating or marked change of heart rate Unconsciousness is the sole symptom

It is important that patients with this syndrome usually have some organic nervous disease This happened in the first three observations later this syndrome was described in patients with insufficiency of the anterior lobe of the hypophysis and in those with tabes or bulbar paralysis A similar disturbance was observed in Addison s disease but here the pulse rate increases markedly on standing This syndrome was ascribed to a paralysis of the vasomotor nerves but a central hypothalamic lesion or a peripheral disorder of the sympathetic nervous system leading to a disturbance of the regulating reflexes mentioned above seems more probable Sympathectomy for the treatment of hypertension provokes a similar syndrome

Two patients with postural hypotension had a deficiency in release of norepinephrine and epinephrine (Luft and Euler) Perhaps this was secondary to a lesion of the sympathetic nerves

Bandaging the legs epinephrine paredrine prostigmine methyl sulfate and preparations of the anterior lobe of the hypophysis have been recommended Bandaging and paredrine are more effective than the others

Carotid Sinus Syndrome

It has been known for a long time that pressure at a certain area in the neck may cause syncope The pressure may be exerted manually by a tumor by instruments during an operation or by certain positions of the head This event was clarified by Hering s discovery of the carotid sinus reflexes Several instances of this type of fainting were published and the syndrome received general recognition after the studies of Weiss and his co workers were published

In some individuals increased sensitivity of the receptors in the carotid artery of the central synapses the efferent neurons or an abnormal condition of the effector organ the heart may produce an abnormal effect consisting of syncope following slight mechanical pressure on the carotid sinus In patients with this affection stimulation of the carotid sinus receptors may be evoked by holding the head in certain positions or by turning the head even pressure of the collar may suffice to produce syncope Similar attacks can be readily elicited

by the examining physician when he exerts pressure on the carotid sinus The attack develops after pressure is applied for 4 to 40 seconds on the right or the left carotid sinus Spontaneous attacks last for one half to three minutes and are sometimes preceded by an aura consisting of dizziness epigastric pain or weakness Later pallor appears with loss of consciousness and convulsions which may be generalized The tongue is not bitten and sphincter control is retained Mental confusion hallucinosis and amnesia are common temporary after effects

Analysis of the cardiac and blood pressure phenomena during the syncope led to the separation of three groups of cases (Ferris et al)

(1) Syncope due to cardiac standstill caused by inhibition of impulse formation

(2) Syncope due to an abnormal vascular reaction which causes the blood pressure to fall to an abnormally low level This and the preceding type were anticipated on the basis of facts known about the physiology of the carotid sinus Of great interest however is the third variety the so called cerebral group'

(3) Syncope that appears with normal or almost normal blood pressure and a normal heart rate In this type unconsciousness occurs as early as four seconds after stimulation of the carotid sinus Originally these attacks were ascribed to focal cerebral vasoconstriction but proof to support this conception could not be obtained The existence of an area for the maintenance of the conscious state which can be influenced by reflexes from the carotid sinus was suggested as a possible explanation

An abnormally functioning circle of Willis is probable the cerebral circulation becoming insufficient when one carotid artery is occluded

Denervation of the carotid sinus by operation the infiltration with novocaine or irradiation of a tumor pressing on the carotid sinus may abolish the attacks for a time Recurrences are not rare and it is difficult to explain them after the carotid sinus nerves have been severed

It should be stressed that many patients with the carotid sinus syndrome either have evidence of a myocardial lesion or else are of an age (over 60 years) when such a lesion could be expected This might be anticipated for two reasons

a Vagus effects on the heart i e vagus inhibition are more pronounced in a damaged heart than in a healthy one a fact repeatedly confirmed since Wenckebach s original report Experimental corroboration is easily secured and the event has become thoroughly comprehensible since the chemical mediation of vagal effects was discovered by Loewi A heart already in a poor metabolic state will respond longer and more strongly to released acetylcholine than a normal one

b In many cases however the stronger effect of vagus stimulation is apparent rather than real In the normal heart the higher atrial centers are inhibited by vagal stimulation while the lower ventricular centers are not influenced Therefore these low centers immediately form stimuli if the higher centers are restrained and thus a serious ventricular standstill is prevented Accordingly healthy people have only a slight slowing of the heart rate during carotid sinus pressure

If an electrocardiogram is taken simultaneously it reveals that the sinus node action is completely inhibited and that ventricular centers beyond the reach of the vagus form stimuli for the ventricle In cases of a myocardial lesion however the deeper centers are damaged they do not escape immediately and prolonged cardiac standstill results

It is therefore a mistake to designate every marked effect of carotid pressure as a carotid sinus syndrome and as evidence of hypersensitivity of the receptors in the carotid sinus or hyperexcitability of some other part of the reflex arc Abnormality of ventricular centers may be responsible

Fainting due to Various Other Mechanisms

In another group of patients cardiac standstill results from other nervous reflexes and disorders While these patients have often been considered to have a nervous type of Stokes Adams syndrome in a majority of cases the modern cardiologist would undoubtedly discover an intrinsic heart lesion as the etiologic factor In many reported cases the examination during life and after death was superficial Thus in a case of a seventy two year old man the attacks of unconsciousness were attributed to a bronchogenic carcinoma which enclosed the vagus nerve Electrocardiograms disclosed a sino atrial block and Stokes Adams attacks *due to sino atrial block is a more probable explanation* *The attacks produced by* reflexes from other parts of the body for instance cardiac standstill on swallowing also belong to this group They have been discussed in a preceding chapter

MORGAGNI STOKES ADAMS SYNDROME

Nomenclature

The occurrence of epileptiform attacks with a slow (radial) pulse was reported by Morgagni (1761) Adams (1827) and other observers Since the paper of Stokes (1846) on this subject was of major importance and had the greatest influence it has repeatedly been proposed to call the syndrome Stokes Adams attacks

Some authors apply this term only to attacks occurring in patients with heart block Cases of circulatory standstill without block e g paroxysmal tachycardia or ventricular fibrillation must have a separate designation In the present volume the term Morgagni Stokes Adams attacks will apply to all type resulting from a change of cardiac activity regardless whether they are due to cardiac standstill or tachycardia Attacks in which cardiac stand till is not the result of an abnormal intrinsic cardiac mechanism (abnormal carotid sinus reflex or instances of abnormal vagal reflexes) are excluded We deal with a syndrome and not a disease entity

Symptoms and Signs

The syndrome occurs if the cerebral circulation is arrested for a certain period If the standstill of cerebral circulation lasts only a few seconds *the patient* is unaware of any disturbance It requires an arrest of longer duration at least

6 to 8 seconds to provoke the sensation of darkness in front of the eyes After the standstill lasts for approximately 10 seconds the patient loses consciousness he becomes pale his eyes turn upward and with continued arrest of cerebral blood flow twitching of the arms and legs begins culminating finally in tonic clonic convulsions Urine and stool are evacuated involuntarily An arrest of circulation lasting more than four minutes is often fatal With the resumption of the normal blood supply the face becomes red and a short period of dyspnea develops A respiratory disturbance similar to Cheyne Stokes breathing occurs if one attack quickly follows another

The attack may occur once and never recur or there may be hundreds of them every day If the attacks are brief the patient may be unaware of them and he may continue a conversation from the point reached when fainting occurred After a long attack with convulsions extreme weakness may follow for a few hours Vomiting is not unusual If one attack succeeds another at short intervals the patient may remain semi conscious or somewhat hazy

Mechanism of the Attacks

The syndrome may be produced by two radically different events whose distinction is important with respect to therapy

Ventricular Standstill (*Cardiac Arrest*) In this form there is actual ventricular standstill Various subgroups are known Most frequently ventricular standstill occurs in disturbances of atrioventricular conduction when the atrial stimuli fail to reach the ventricle If the lower centers are normal they immediately start functioning when the conduction of stimuli to the ventricle stops As pointed out earlier however these lower centers are also affected in many patients and a certain time elapses before they can develop their automatic activity The clinical manifestations depend upon the duration of the pre automatic pause or stoppage of the ventricles until the activity of the lower centers begins Therefore in order for this form of Stokes Adams to appear two disturbances are necessary failure of the atrioventricular conduction and failure or retarded development of ventricular automatism

In a majority of patients who develop atrioventricular block the automaticity of the ventricular centers is normal and therefore cardiac arrest appears only in a small percentage of patients with heart block

Since complete heart block is usually transient at first and conduction is temporarily reinstituted only to fail again such attacks often recur If the history of patients with heart block is carefully recorded one notes that for some time the patient has suffered from attacks of vertigo and fainting It may safely be assumed that heart block developed precisely at that time

Rapid Ventricular Activity This form of Morgagni Stokes Adams syndrome formerly regarded as rare but actually common is caused by attacks of tachycardia The faster the cardiac rate the shorter diastole and the smaller the stroke volume If the rate of the heart exceeds a certain limit the period available for cardiac filling becomes too brief and the ventricles expel so little blood

with such feeble force that the circulation for practical purposes is at a standstill or at least is reduced to a minimum With a good cardiac muscle and healthy vessels young people tolerate an extremely rapid ventricular rate even more than 300 per minute very well Older people with sclerotic vessels or patients with myocardial disease or a valvular lesion with predominating stenosis — the latter resulting in a small stroke volume from the start — may exhibit disturbances of cerebral circulation with a tachycardia of much lower rate These disturbances may cause temporary vertigo or hemianopsia (Barnes) Prolonged unconsciousness without convulsions may be noted when some cerebral circulation is maintained Hemiparesis which vanishes promptly when the tachycardia stops is also observed In short the cerebrum like the heart responds to a tachycardia according to the state of its vessels

Very often the tachycardia evoking this syndrome is due to paroxysmal atrial fibrillation a common event in patients with coronary sclerosis If transient attacks of ventricular fibrillation are not lethal the effect on the circulation is identical with that of complete cardiac standstill Scott and Sancetta observed Morgagni Stokes Adams attacks caused by ventricular tachycardia in a patient with A V block they were elicited by mechanical rectal irritation

Syncope d effort (Calliavardin) is usually caused by ectopic arrhythmias

Differential Diagnosis

This is difficult for many reasons Examination of the patient between the attacks may not permit a decision in both major varieties Differentiation may be impossible even when the patient is seen in an attack The patient may be pulseless and may show a cadaveric pallor in complete ventricular standstill as well as in ventricular fibrillation The heart sounds are often inaudible in patients with rapid ventricular activity or ventricular fibrillation on the other hand rapid rhythmic sounds caused by the contraction of the atria may be audible during ventricular standstill For this reason an electrocardiogram of the patient during the attack is indispensable in many cases to establish the diagnosis If the attacks recur at irregular intervals and without warning this may be impossible

Moreover the presence of some irregularity of rhythm between the attacks does not aid in differentiation One might expect that the first form (ventricular standstill) would occur in patients who exhibit atrioventricular block between the attacks whereas the presence of extrasystoles would be a sign that the attacks are due to a disturbance of stimulus formation (paroxysmal tachycardia or fibrillation) Recent experience has taught however that the combination of both forms often occurs and even during the same attack patients may have ventricular tachycardia or ventricular fibrillation *and* complete ventricular standstill

Three causes are known for such an event The tachycardia may follow standstill because ventricular inactivity leads to an accumulation of metabolites

in the centers this stimulates them and evokes a tachycardia At other times cardiac standstill follows a tachycardia because overactivity fatigues the centers and inhibits their automaticity Finally attacks of ventricular fibrillation and polyfocal ventricular extrasystoles are particularly common in patients with complete heart block presumably because the same lesion usually coronary sclerosis which causes the block also produces irritation of the specific fibers and leads to abnormal stimulus formation A bilateral bundle branch block is often present

Figure 88 was obtained from a patient with coronary sclerosis and complete heart block The patient suffered from typical Stokes Adams attacks with convulsions The electrocardiogram registered repeatedly during the attacks showed that they were due to ventricular fibrillation In figure 88 the complete heart block is interrupted by a group of 13 multiform ventricular extrasystoles Such short attacks often preceded or followed typical ventricular fibrillation in *this patient*



FIG 88 Complete atrioventricular block and brief ventricular tachycardia with variform ventricular complexes

The differentiation of these attacks from epilepsy hysteria and the attacks of syncope discussed in the preceding section is not always easy Many patient with Stokes Adams syndrome whom we have had an opportunity to see originally consulted a neurologist for epilepsy and some of them were treated for this disease If in the midst of seemingly perfect health a patient suddenly becomes unconscious and has convulsions such an erroneous diagnosis is comprehensible

Prognosis

The outcome depends upon the underlying disease and the mechanism responsible for the attack In a majority of cases the attacks are due to coronary sclerosis We are dealing with a serious complication and sudden death is common *Patients who have these attacks may recover and lead a useful life* for many years with or without complete heart block In one personally observed case in which Stokes Adams attacks followed coronary occlusion hundreds of such attacks appeared daily for many days but the patient was seen alive and well four years later When the attacks are due to ventricular fibrillation the prognosis is much worse than it is in ventricular standstill

Treatment

Therapy should not be started until it has been determined whether the attacks are caused predominately by tachycardia (or fibrillation) or ventricular standstill Treatment without a conclusive diagnosis may result in a serious and even fatal outcome (Scherf) The remedies required in one form possess actions that are injurious in the other If cardiac standstill is present stimulants must be given which would be fatal in the tachycardias and in ventricular fibrillation *On the other hand depressants like quinidine so effective in the* tachycardiac form can induce serious injury if the attacks occur because of standstill Furthermore it seems that quinidine enhances the development of ventricular fibrillation in these cases (Schwartz) Since both types may appear successively in the same patient it is often safer to withhold treatment

In the therapeutic program a distinction should be made between measures indicated in the attack and measures aimed at the prevention of recurrences

Cardiac Standstill If the attacks are due to cardiac standstill and the patient is seen during an episode an immediate attempt to excite ventricular automatism should be made Many times this can be accomplished simply and rapidly by means of sharp blows or slaps to the cardiac area In animal experiments when the heart is exposed a quick blow on the heart with a blunt instrument almost always leads to the desired effect and automaticity starts anew

The intracardiac injection of epinephrine may be lifesaving but often the *effect is too violent and there is considerable danger that ventricular fibrillation* will replace cardiac standstill For this reason caffeine sodium benzoate is more worthy of recommendation for intracardiac injection Often pricking of the heart with the needle suffices to awaken automatism For prevention if one attack succeeds another at short intervals epinephrine may be given (0 2 ml of the standard solution) subcutaneously with good results Ephedrine in tablets of 30—60 mg three times daily is often useful in preventing attacks caused by ventricular standstill Norepinephrine like epinephrine creates ectopic rhythms and its administration in form of infusions is difficult Isuprel which can be given in the form of linguets (10 mg) is in our experience a useful agent (Nathanson and Miller)

Atropine formerly employed without discrimination in all cases of heart block is effective only when the attacks are caused by abnormal vagal reflexes

Barium chloride has also been recommended for the treatment of attacks of cardiac standstill This usage is based on the experimental observation that the compound actually increases the automaticity of the cardiac centers in a very remarkable manner and causes abnormal impulse formation The dose is 40—50 *mg of barium chloride that is 20 drops of a 5 per cent solution* by mouth three times a day This therapy is not devoid of danger Barium chloride is absorbed from the intestine with great variability in different individuals and the borderline between the effective and the toxic dose is very sharp Accordingly no reaction occurs in some cases until a ventricular tachycardia suddenly appears We do

in the centers this stimulates them and evokes a tachycardia At other times cardiac standstill follows a tachycardia because overactivity fatigues the centers and inhibits their automaticity Finally attacks of ventricular fibrillation and polyfocal ventricular extrasystoles are particularly common in patients with complete heart block presumably because the same lesion usually coronary sclerosis which causes the block also produces irritation of the specific fibers and leads to abnormal stimulus formation A bilateral bundle branch block is often present

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Cardiac Resuscitation In recent years cardiac accidents during anesthesia and surgery have become more common This is partly explained by the increased number of chest and cardiac operations Cardiac standstill occurs when the pleura or the pericardium is opened or when a bronchus or a large blood vessel is ligated In the section on vago vagal reflexes other instances are mentioned Cardiac standstill is observed with increased frequency also because of the pre anesthetic medication used in many institutions in ever increasing amounts Quinidine atropine barbiturates and procaine amide have been recommended They all depress *automaticity of the ventricular centers so that they do not develop their own rhythm* when the higher centers are inhibited The depressed automaticity of the deeper centers is presumably the chief reason that cardiac arrest occurs five times more often in patients with cardiac disease

Ventricular contraction may stop because of intrinsic heart disease or as a consequence of inhibiting vagal reflexes Cardiac standstill has been seen in patients with glosso pharyngeal neuralgia it has been observed during swallowing (Adamson et al)

The same effect (standstill of the circulation) is observed when ventricular fibrillation sets in The treatment is of course very different from that of cardiac standstill

Cooley found it necessary to employ cardiac resuscitation in 48 of 878 patients operated on for pulmonary stenosis Circulation was restored in 33 with normal cardiac action but only 12 survived It is estimated that in 90 per cent of these patients we are dealing with cardiac asystole and in 10 per cent with ventricular fibrillation Others estimate an incidence of cardiac arrest once in 1000—5000 anesthesias (Singleton and DeLoach)

A differentiation between the two forms is possible only with electrocardiogram or inspection of the exposed heart The latter must be employed in practically all cases unless the electrocardiogram is observed continuously during surgery as too much valuable time would be lost in setting up and taking the electrocardiogram Heart sounds are heard on auscultation in both conditions because of the continuous activity of the atria

The immediate therapy consists of two measures and is the same in both conditions *first exposure of the heart (if it is not already exposed) to permit massage* second artificial respiration and supplying oxygen which the anesthetist does best with an intratracheal catheter

The chief principle is the restoration of circulation by massage within 3 minutes Any delay beyond this time may save the patient but the damage to cortical centers may make them vegetating mental cripples with multiple neurologic manifestations no longer useful members of society In cyanotic or *decompensated patients damage to the centers has been observed* after a standstill of the circulation lasting only 60 seconds

The anatomist Tandler stated in connection with another emergency operation that three things are necessary for it courage a sharp knife and some anatomic knowledge Without regard to asepsis or bleeding a deep cut is made in

the fourth intercostal space and the hand of the physician is forced through it massage of the heart — which is placed between the thumb and other fingers — is started and performed 50 to 60 times a minute The finger readily detects the presence of either cardiac standstill or the characteristic sensation noted when a fibrillating ventricle is massaged the sensation of thousands of worms continuously wriggling Simultaneously 100 per cent oxygen is supplied by a respiratory or tracheal tube or as an emergency by mouth to mouth breathing

In vago vagal standstill the heart often beats immediately after the massage is begun Atropine may be given in small doses Calcium recommended by Blalock has the danger of inducing ventricular fibrillation as has barium suggested by Fauteux Adrenaline also often leads to fibrillation but caffeine sodium benzoate or Isuprel sublingually may be used with advantage

A new method is electric shock treatment (Zoll) which may cause unpleasant burning and twitching of the skin but otherwise is useful

When fibrillation of the ventricles is present the administration of quinidine or Pronestyl has disadvantages since these drugs depress ventricular automaticity so that the end of fibrillation may be followed by standstill The instillation of Pronestyl into the pericardial cavity causes the same effect as an intravenous injection since the compound is absorbed with amazing speed The best success is accomplished with the electrical devices designed for defibrillation An alternating current of 110 – 135 volts with a current flow of one or more amperes is used repeatedly for less than 0 5 second Often higher voltage is necessary but it may cause burns Voltage of less than 100 may cause fibrillation Electric countershock applied externally helped 11 times in 4 patients (Zoll)

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Chapter 23

Aortitis

Described for the first time more than 80 years ago (Welch Dohle) aortitis has been recognized for many years as one of the more common cardiovascular lesions For a long time atherosclerosis which so often accompanies aortitis obscured the diagnosis of the latter even at necropsy Careful histologic examinations disclosed that many museum specimens of atheroma and atherosclerotic aortic regurgitation represented in fact cases of syphilis and syphilitic aortitis

Incidence

Figures concerning the incidence of syphilitic aortitis vary in accordance with many factors the chief of which is the prevalence of syphilis in the community As might be expected the condition is more common in metropolitan areas than in some rural areas More cases will be seen in seaports and in cities with a large colored population The incidence of the disease has been markedly diminished with better treatment of early syphilis and some complications like aortic aneurysm are decidedly less common than they were about 20 years ago as is seen in the following statistical data

In several series of more than one thousand consecutive autopsies before the introduction of penicillin the incidence of aortitis in different parts of the world was found to be 3 6 4 93 6 5 6 89 and 7 per cent

It has been estimated that aortitis was present in 70 to 80 per cent of all syphilitic bodies coming to autopsy However Carter found an incidence of only 22 2 per cent It was estimated that 30 000 to 40 000 persons died each year in the United States from aortitis before the introduction of the antibiotics In untreated syphilis the cardiovascular system was involved in 13 6 per cent of the men and 7 6 per cent of the woman (Clark and Danbelt)

The incidence of syphilitic cardiovascular lesions among patients with organic heart disease has been found in some hospitals to amount to 5 to 15 per cent After arteriosclerosis hypertensive heart disease and rheumatic fever syphilis was the most common etiologic factor for cardiovascular disease

In the colored population its incidence is about three times as great as in the white The lesion occurs in women as often as in men

Pathology

The process begins in the adventitia and media as an endarteritis of the vasa vasorum. It involves chiefly the first 5—8 cm. of the ascending aorta and usually but not invariably ends sharply where the descending aorta begins. There is perivascular infiltration with round cells and plasma cells; necrotic areas appear in the media. Primary involvement of the intima is rare. The small necrotic areas weaken the media and may lead to aortic dilatation and the formation of an aneurysm. The inflammatory process in the adventitia leads to adhesion between the ascending aorta and neighboring tissues which permit the diagnosis even before the aorta is opened. The destructive medial process causes intimal depressions which are characteristic in the earlier stages. Later, with the development of fibrosis and secondary lime salt deposits, it is sometimes difficult to make the correct diagnosis without histologic examination.

Adhesions between the lateral parts of the aortic leaflets and the intima of the aorta cause the commissures to widen and the leaflets to separate from each other. This leads to aortic insufficiency. The process in the aorta around the coronary orifices often narrows the ostia and even causes their complete occlusion although the coronary arteries themselves are not involved.

There is no proof that atherosclerosis of the coronary arteries occurs more frequently in patients with syphilitic cardiovascular disease than in others. Arteriolar changes, however, have been described in syphilitic infection (Love and Warner). They consist in thickening of the media and intima. A high incidence of marked peripheral vascular sclerosis in colored patients with aortitis has been noted (Cannon). The formation of a gumma in the myocardium is not common and syphilitic myocarditis is a great rarity.

Symptoms

Aortitis is often described as an asymptomatic disease. As a matter of fact the process often becomes very advanced without the patient having any symptoms. Frequently the lesion is discovered only on the occasion of a routine examination. Heart failure in connection with a syphilitic aortic regurgitation, angina pectoris, syphilitic coronary stenosis, or pressure phenomena due to an aneurysm often provide the first evidence of the disease. With one possible exception, which is discussed below (aortalgia), the symptoms depend upon the complications of aortitis and not on the aortitis itself.

Many patients are surprised by an attack of nocturnal dyspnea or exertional dyspnea. In other instances, peripheral edema and swelling of the liver force the patient to seek medical aid. In a third group the typical anginal pain on effort is the outstanding symptom.

Aortalgia. Still a subject of dispute as a more or less characteristic symptom of aortitis is aortalgia, or aortic pain. Pain of an anginal type may originate in the sensory fibers of the ascending aorta. This explanation seems particularly adequate for the continuous burning sensation behind the sternum occasionally

encountered in cases of aortitis when inflammatory processes exist in the adventitia. This sensation lasts for months and is slightly aggravated by effort. It usually disappears as the lesion progresses, for presumably the sensory nerve fibers are destroyed. We have found this sensation in a small percentage of patients with aortitis, but its existence or the existence of any painful sensation in aortitis without coronary involvement is denied by others (Giertsen, Mattman and Moore).

In cases of aortitis with attacks of paroxysmal nocturnal dyspnea, the complaint of substernal pain at the time of the attack is very common. This complaint is so typical that the suspicion of aortitis is justified in patients who complain of dyspnea and substernal pain at the same time, provided a coronary occlusion can be ruled out. The rise of blood pressure during the attack of paroxysmal dyspnea may in some way be responsible for the simultaneous pain.

Signs

The diagnosis in a typical case is easy because a characteristic syndrome may be present. No sign, however, is pathognomonic and none is invariable. Any single sign occurs only in a certain percentage of cases, so that great difficulties may arise concerning the diagnosis of the lesion and its differentiation from other processes. In many instances the diagnosis is presumptive rather than established.

Abnormal Pulsations. The enlargement of the aorta leads to an increased dullness over the manubrium sterni if the aorta approaches this site over a greater area than normal. The aorta frequently elongates as well as dilates, leading to the appearance of strong pulsations in the jugular notch. The innominate artery now originates higher than normally, the course of the right subclavian artery is higher, and the right carotid artery undergoes some kinking. These pulsations are often confused with aneurysms. They are also found without aortitis if atherosclerosis is present.

Often the closure of the aortic valves is palpable slightly to the right of the sternum in the second or third interspace. This pulsation naturally is found not at the site of the aortic valves but where the ascending aorta approaches the chest wall. While not characteristic of aortitis, this phenomenon otherwise is rarely encountered, since marked aortic dilatation with accentuation of the second aortic sound are necessary for its appearance. It is very rare, therefore, in simple hypertension. If the phenomenon is found in patients under 50 years of age, aortitis should be suspected.

The frequent narrowing of the orifice of the large arteries originating from the ascending aorta (innominate, left carotid, and left subclavian artery) by the syphilitic process leads to marked difference in the pulses of the right and left sides. Complete or almost complete disappearance of one carotid pulse or one brachial pulse with a difference in blood pressure is not rare and also permits the diagnosis. These signs often are mistakenly considered to be evidence of aneurysm. Actually they are common in uncomplicated aortitis.

Percussion In many cases percussion reveals no cardiac enlargement while in others marked dilatation to the right and left with an aortic configuration or mitralization of an aortic heart appears This occurs if hypertension aortic regurgitation or narrowing of the coronary orifices complicates aortitis

Auscultation The second aortic sound is often changed It is accentuated and ringing (tambour like drumlike tympanitic hollow) This change presumably the result of anatomic changes in the aortic wall is not peculiar to aortitis for it may be encountered in patients with atheromatosis of the aorta and hypertension with sclerotic changes of the aortic wall In pure hypertension there is only an accentuation of the second aortic sound without a tympanitic or bell like character If discovered in patients under 50 without hypertension the sign is a very strong argument in favor of the diagnosis of aortitis

Usually a systolic murmur due to eddies caused by the dilatation of the vessel is audible over the aorta Often this systolic murmur is also heard at the apex and should not be confused with a mitral murmur

Blood Pressure The blood pressure is often increased Systolic blood pressure values over 150 are found very often in patients with aortitis (Boyd and Scherf) We would estimate that hypertension is present in about 50 per cent of the fully developed cases in the white race In the colored group the percentage is higher This elevation of blood pressure is interesting since no relation between syphilis and essential hypertension seems to exist The systolic hypertension is usually the consequence of lost elasticity of the ascending aorta The diastolic pressure is also increased in a majority of cases An explanation for the diastolic hypertension in aortitis is still lacking

Other Findings Evidence of neurosyphilis is often found In some observations it was present in 26 per cent of the cases

The serologic reactions are positive in about 80 per cent of cases percentages of positive reactions of 86 per cent (Beckh) and even 92 6 per cent (Carter and Baker) have been reported The spinal fluid is abnormal in almost 50 per cent The treponema immobilization test may be positive when the Wasserman reaction is negative

In youthful patients with severe rapidly progressing aortitis elevation of the temperature to over 38° C has been observed If an aortic regurgitation coexists the erroneous diagnosis of subacute bacterial endocarditis is often made

The erythrocyte sedimentation rate is often accelerated but this finding is rarely of diagnostic value

Frequently in aortitis — as in aneurysm — sensitivity to percussion is elicited over the spinous processes of the second to fourth thoracic vertebrae

Roentgen Examination and Fluoroscopy These examinations greatly aid in the diagnosis One of the earliest signs is a dilatation of the ascending aorta particularly in its first portion Prominence of the aortic arc at the upper right cardiac border if found in a person under 40 years of age without a high diaphragm or coarctation is a very suggestive and helpful finding Dilatation of the

aorta may however be absent or may be missed since the supravalvular part of the vessel is hidden in the cardiac shadow

It is important to stress that even in patients with fully developed aortitis or syphilitic aortic insufficiency evidence of aortic dilatation and elongation is not necessarily present if the process involves only the portion of the aorta situated around the valves and the orifices of the coronary artery without spreading upward

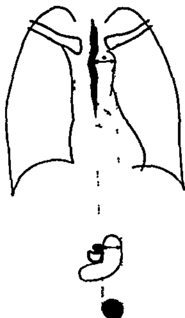


FIG 89



FIG 90

FIG 89 Measurement of the diameter of the arch of the aorta by the Kreuzfuchs method (Zdansky)

FIG 90 Calcification of the ascending aorta and aortic arch in a patient with syphilitic aortitis

The diagnosis of an aortic dilatation should never be based on measurements of the vascular band in the postero anterior projection Examination in the oblique positions is necessary and very informative Unfortunately exact measurements of the width of the aorta in its different portions is not possible The most reliable method is that of Kreuzfuchs by which the width of the part of the aortic arc forming the aortic knob can be estimated This method is based on the fact that one part of the aortic arc takes a purely sagittal course and lies close to the esophagus even causing a light impression on it with a displacement from left to right (figure 89) This indentation is easily seen if a contrast medium of barium is swallowed by the patient First the point of the aortic knob which

is the farthest to the left during systole is found and marked orthodiagraphically on the screen then the deepest point of the 'aortic bed of the esophagus is found while the patient swallows the barium

The diameter of the healthy aorta ascertained in this way is 1 8—2 5 cm Patients over 60 years of age may have values up to 3 cm Some authors recommend the deduction of 2—3 mm for the thickness of the esophageal wall periesophageal connective tissue mediastinal pleura and the double thickness of the aortic wall Since all these values are relatively constant it has been proposed that the deduction be omitted

In addition to the aortic dilatation the discovery of lime salt deposits in the aortic knob is common (figure 90) The frequent appearance of these calcified placques in aortitis is ascribed to the great incidence of secondary calcification in the involved tissue of the aortic wall The appearance of this sign in patients under 50 years of age is also a strong argument in favor of the diagnosis of aortitis

Angiocardiography In some instances this has revealed an irregularity of the lumen variations of thickness of the wall of the aorta and tortuosity

Electrocardiogram While the electrocardiogram furnishes no diagnostic help it is significant for prognosis since it aids in establishing the diagnosis of a complicating coronary stenosis The discovery of a simple left axis deviation or of a normal electrocardiogram may indicate a healthy myocardium while in many patients with few complaints and scanty objective findings abnormal T waves in each lead and widening and slurring of the QPS complexes indicate a serious myocardial involvement and a bad prognosis Often coronary stenosis can be diagnosed from the alterations of the electrocardiogram after exercise in patients who show a normal electrocardiogram at rest (Scherf)

Complications

Aortic Regurgitation One of the most common complications of simple aortitis is insufficiency of the aortic valves its symptomatology was discussed in connection with rheumatic aortic regurgitation Most of the findings are common to both lesions and the differentiation may be very difficult in some cases when a history of rheumatic fever or syphilitic infection is absent Furthermore the serologic reactions may be negative in syphilis and may be positive in patients with rheumatic aortic regurgitation The presence of narrowed orifices of the large arteries (differences in the pulsations of both carotid or both brachial arteries) is evidence of aortitis

It should be remembered that a rheumatic and syphilitic involvement of the aortic valves may coexist

Of great help is the old rule that the marked dilatation of the aorta in syphilitic aortic regurgitation permits the diastolic murmur in this lesion to be conducted better to the second right intercostal space while in rheumatic aortic regurgitation it is heard better at the lower left sternal border Although exceptions do occur the rule has clinical value

Aneurysms Aortic aneurysm another complication of aortitis will be discussed under a separate heading

Stenosis of the Coronary Ostia The third and most dreaded complication narrowing of the orifices of the coronary arteries is also of great importance It is a common event for it was found at postmortem examination in every third or fourth case of aortitis (Clawson) Often both orifices are involved sometimes one orifice is completely occluded and the other is just patent for a head of a pin or merely for a bristle Aortitis was presumably present in one of the oldest published cases of this type (Crooke) In a series of 1000 consecutive necropsies aortitis was present in 69 instances (Pincoffs and Love) In 15 of these 69 observations coronary stenosis was found Eight times both coronary arteries were involved in six instances only the right and in one case only the left was narrowed It is significant that 10 of these 15 patients died suddenly Woodruff found coronary stenosis in 27 per cent of aortitis discovered incidentally It was present in 57 per cent of those cases in which aortitis was diagnosed clinically because of symptoms In 39 per cent of these stenosis of both ostia was found

Stenosis of a coronary orifice or even its complete occlusion due to syphilitic aortitis is often tolerated without symptoms These changes are found accidentally at post mortem and were never suspected during life They must have existed for some time since the occlusion is created by old scar tissue The slow development of the coronary occlusion permits sufficient widening of a collateral circulation

The frequent occurrence of pain (decubital angina) in some cases may be considered as a sign indicative of coronary involvement In the majority of cases only pain on exertion i e typical effort angina exists and in these cases if aortitis is present one is permitted to assume a narrowing of the coronary ostia without further evidence Infarction of the heart muscle in cases of aortitis and coronary stenosis or occlusion is rare It is interesting that in these cases cardiac hypertrophy rarely develops (Cannon) presumably because of the diminished blood supply Furthermore dilatation of the heart and conduction disturbances in the electrocardiogram may be absent showing that the slow development of a syphilitic coronary obstruction allows ample time for the development of a collateral circulation and to provide sufficient blood supply to the specific tissue of the heart (Scherf and Boyd)

Syndromes have been described which may lead to the diagnosis of coronary stenosis in aortitis The rapid course of the lesion from the beginning of symptoms the lack of response to treatment the prominence and high incidence of anginal pain and the frequency of sudden death often permit the diagnosis of coronary stenosis In another group the diagnosis of marked stenosis of the coronary ostia confirmed at necropsy was made in four cases on the basis of the following syndrome (van Muijden and Scherf) An aortitis was present with or without aortic regurgitation The heart was normal in size or moderately enlarged The patients complained of pain behind the sternum and between the shoulders or

upper abdomen occurring on slightest exertion or excitement as well as frequently at rest and without apparent reason There was great anxiety and apprehension This anxiety may be the chief complaint in the absence of all other symptoms The anxiety was associated with an inexplicable restlessness All these complaints were immediately abolished by nitroglycerin In these cases the blood pressure rose only slightly during an attack of anginal pain in more advanced stages it fell sometimes to very low values This fall of blood pressure may precipitate a state of anxiety The slightest exertion leads to marked changes of the RS T segments and the T waves in the electrocardiogram

In patients with complete occlusion of only one coronary orifice and normal width in the other a normal electrocardiogram may be obtained even after exercise (Scherf)

Congenital Syphilis and Aortitis

Aortitis is rare in cases of congenital syphilis but many verified instances have been reported The affection of the aorta with the typical inflammatory changes in the media and adventitia was described long ago It seems that in most cases reparative processes take place if the child survives the first year and only exceptionally is there a progressive lesion with aneurysmal formation coronary stenosis or the development of an aortic regurgitation The lesion has been observed in a brother and sister with congenital syphilis (McDonald) In spite of the great tendency to spontaneous recovery the possibility of aortitis due to congenital syphilis must be considered in children and juveniles when the symptoms and signs discussed above are present

Course and Prognosis

The aorta seems to be infected within 12 months whenever treatment is insufficient (Coombs) Some evidence of an aortic lesion has been described as early as six to seven months after the infection (Carter and Bykcr Wile) but in a majority of cases years and even decades elapse before definite evidence of aortic disease appears In 10 per cent of a large series of cases the infection dated back less than five years (Cole and Usilton) An interval of 16 or even 20 years between infection and discovery of the first evidence of the disease is not rare but an aortitis might have existed for a long time before it was discovered

Of paramount importance is the fact that very benign cases exist and the disease may cease to progress at any stage It may remain asymptomatic or may run a very rapid course within a few weeks We have seen patients who claimed they felt normal until two or three weeks prior to the first examination yet who developed congestive heart failure did not respond to treatment and died a few weeks later Very often aortitis is an accidental finding at necropsy In patients who die from extracardiac causes a few suspicious spots may be seen in the aorta at necropsy on gross examination and only histologic examination confirms the diagnosis of syphilitic aortitis In many statistics compiled by pathologists these cases are included

The condition of the myocardium and of the orifices of the coronary arteries is of major importance for the prognosis If the orifices of the coronary arteries are narrowed sudden death frequently occurs Even if there is no history of anginal pain and the electrocardiogram is normal the tracings obtained after an exercise test may reveal a marked coronary stenosis

Because of modern therapy the statement that aortitis is ubiquituous insidious and disastrous is perhaps no longer correct The prognosis is said to be worse in colored patients and in those who are engaged in hard manual labor

Differential Diagnosis

In typical cases the diagnosis is easy For example a forty year old man or woman has a history of a syphilitic infection the serologic reactions are positive and the patient complains of anginal pain on effort Examination reveals a markedly widened aorta prominence of the ascending aorta to the right on x ray examination a tympanitic second aortic sound a rough systolic murmur over the aorta and scarcely palpable pulsations of the left carotid artery whereas the right pulsates strongly

However it has been stressed earlier that none of these signs is obligatory in aortitis Typical cases such as the one indicated above are exceptional The history and serologic tests may be negative and most of the signs mentioned may be absent Often the condition is oligosymptomatic and the positive diagnosis is difficult

In many patients under 50 (the younger the more surely) a dilatation of the ascending aorta calcification of the aortic knob a suspicious accentuation of the second aortic sound a systolic murmur over the aorta evidence of left ventricular hypertrophy and dilatation in the absence of hypertension lead to the correct diagnosis

Difficulties arise from the fact that hypertension is common in aortitis and practically all signs found can be attributed to the increased blood pressure alone This frequent combination of hypertension with aortitis makes it obligatory to consider aortitis in every hypertensive patient in whom no cause for the hypertension is found and in whose family there is no history of hypertensive disease However even if the possibility of an aortitis is considered it may be difficult or impossible to prove

Another problem arises in patients over 50 since we must differentiate between aortitis and atheroma If one realizes how difficult it often is even for the experienced pathologist to state on examination of the opened aorta whether a pure atheromatosis or a combination of atheromatosis and aortitis exists one will appreciate the problem the clinician faces In some cases the differentiation is possible only by histologic examination It is because of this frequent combination of aortitis with atheromatosis that the clinical and even the pathologic picture of aortitis described so many years ago found general recognition relatively late The widened aorta lime salt deposits in the aortic knob and the systolic

murmur in this area can be fully explained by the atheromatosis The same is also true of the elevated blood pressure in certain cases

Figure 90 shows calcium deposits in the ascending aorta and in the aortic knob in a 52 year old patient with syphilitic aortitis and an aortic regurgitation

All this leads to great diagnostic difficulties certainly in many cases the diagnosis is impossible But the number of correct diagnoses increases in many institutions whenever the rules discussed in the previous paragraphs are heeded On the other hand there are some investigators who assert that the diagnosis of uncomplicated aortitis is for practical purposes impossible (Kampmeier et al)

Midway between those who maintain that it is impossible to diagnose the lesion and those who risk making the diagnosis in patients with a simple atheromatosis there are authors who think the diagnosis is permissible only if (1) syphilis exists beyond any doubt (2) the aorta is definitely dilated (3) no other reason for aortic dilatation exists and (4) the patient is not over 40 years of age It is clear from the preceding discussion that the number of patients who fulfill these conditions is limited

If the results of recent investigations prove correct namely that efficient early treatment improves the prognosis prevents complications and prolongs life it is better to make an erroneous diagnosis of the lesion now and then than to overlook it completely because of too rigid criteria

Treatment

Prevention of aortitis in syphilitics seems possible with adequate treatment of the early stages In a large series of syphilitic patients it was found that a satisfactory treatment in the early stages was followed by aortitis in only 1 per cent of cases (Cole and Usilton) In another series (Vonderlehr and Usilton) no patient with cardiovascular syphilis was detected among those well treated and re examined 10 to 20 years after the infection The incidence of aortitis seems to increase in proportion to the inadequacy of the treatment in the earlier stages

Most cardiologists agree that patients with aortitis should receive antisyphilitic treatment If patients exhibiting evidence of aortitis are treated energetically the progress of the lesion seems to be prevented or at least the incidence of aortic regurgitation and aneurysm appears reduced However it is important to consider certain contraindications to treatment One of these is severe cardiac failure In such cases mercurial diuretics which also have an antisyphilitic action may be given In some of our patients an injection was administered weekly for three to five years for its diuretic action with much benefit and without untoward effects We would therefore suggest the consideration of this form of mild antiluetic treatment which also improves the circulation of the patient There are authors however who as soon as evidence of cardiac failure disappears use energetic therapy with penicillin

A very important contraindication is presented by the group of patients with angina pectoris It is assumed that the stenosis of the coronary orifice that exists in these cases will be increased by the treatment because the connective tis

sue will shrink Furthermore hyperemia of the inflamed tissue due to a Jarisch Herxheimer reaction at the beginning of the treatment may also increase the frequency and duration of the attacks Not rarely severe attacks of angina pectoris actually appear for the first time following therapy Observations have been reported however of disappearance of anginal pain during therapy

At present treatment with penicillin has superseded all the other previous therapeutic methods (salvarsan iodine bismuth) Procaine penicillin (1 200 000 units) is given daily until the patient has received six to nine million units Therapy is carried out in the hospital Herxheimer and paradoxical therapeutic reactions are observed regardless of the size of the initial doses No antecedent treatment with iodine is necessary Fever may be observed for a few days Slight decompensation is not considered a contraindication In several cases disappearance of slight anginal pain has been observed Only one series of treatment suffices Every patient with this disease who has not had penicillin before should receive this treatment once

There are no reliable statistics available as yet to prove that the dosage mentioned above suffices or that it stops progress of the illness

Heavy physical labor should be forbidden to patients with aortitis

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Chapter 24

Aneurysms

THE EXISTENCE OF ANEURYSMS has been known since the early description by Galen An aneurysm is a local widening of an artery with partial destruction of its wall there is proliferation of connective tissue from the adventitia and neighboring structures These features separate aneurysms from ectasia and dilatation of the arteries A distinction is also made between saccular aneurysms which are sharply demarcated from the normal part of the vessel and cylindric or fusiform aneurysms in which the separation is gradual although a large segment of the artery is usually involved

Arteriovenous aneurysms are not actual aneurysms and should be called arteriovenous fistulas Dissection of the aortic wall is still often incorrectly called an aneurysm

THORACIC ANEURYSMS

Etiology

The cause for aneurysms varies in different locations Most thoracic aneurysms are undoubtedly the result of syphilis but atherosclerosis bacterial infections (mycotic aneurysm) congenital malformations and trauma also play an etiologic role In recent years syphilitic aneurysms have become rarer while those caused by atherosclerosis are more common Formerly when the histologic changes in the thoracic aorta were studied the syphilitic variety was found in a majority of cases and nonsyphilitic thoracic aortic aneurysms were rather exceptional The incidence of syphilitic aneurysms has diminished in recent years

Aneurysms have been reported in patients with congenital syphilis In acquired syphilis the average time elapsing between the infection and discovery of the aneurysm is about 20 years but cases have been reported in which aneurysms were noted two years (Sanford) after the infection It was pointed out in the chapter on aortitis that syphilitic invasion of the aorta always begins within the first two years after infection

Incidence

In a study of 5000 cases reported in the literature thoracic aneurysm was found to be the cause of death in 0 13 per cent of individuals in large American cities This figure must be amended however since many statistics were compiled by coroners who investigated death under unusual circumstances (Boyd) Irn

spective of its former incidence there is no doubt that energetic treatment of the early stages of syphilis has made the condition much rarer at present

Aneurysm of the thoracic aorta occurs about five times more often in males than in females In Negroes the incidence is about five times higher than in the white population

Aneurysms occur at all ages Examples have been reported in children as well as in men over 90 years of age (Willson and Marcy) The maximum incidence however is between 36 and 40 years in males while in women the peak occurs in a group about 10 years older (Boyd) *In Negro patients aneurysms appear in younger age groups*

Pathology

Usually aneurysms are single but multiple aneurysms are not rare In one series two to five aneurysms were found in 20 per cent of the affected patients (Lucke and Rea) In another series however multiple thoracic aneurysms were seen only 23 times in 633 cases (Kampmeier)

Syphilitic aortitis mainly involves the media Destruction of the muscle cells and elastic fibers weakens the wall so that intra aortic pressure causes bulging The original wall may be completely destroyed and reactive inflammation in the adventitia plus pressure on neighboring tissues causes new layers of fibrotic tissue to form Thrombi develop within the aneurysmal sac and may fill it completely Secondary deposits of calcium in the thrombotic mass and in the remaining parts of the aorta are common

If the thoracic aorta is divided into the ascending aorta the arc the border between the arc and the descending aorta and the descending aorta proper the incidence of aneurysms is 10 to 7 to 3 to 1 respectively Another aid to the understanding of the development of aneurysms in the thoracic aorta is furnished by the so called surge line which connects the sites at which the impact of the blood on the aortic wall is strongest Directly above the valves this area is situated on the anterior wall of the aorta As the aorta ascends this line moves laterally to the right in the arc it is approximately in the center of the vessel passing from here to the left posterior aspect of the wall where the descending portion of the aorta begins In the lower part of the descending aorta it lies in the middle of the posterior wall Although exceptions are not rare this line connects the favorite locations of thoracic aneurysms

Aneurysms of the Sinus of Valsalva Aneurysms of the intrapericardial portion of the aorta may originate from the sinus of Valsalva Often they are very small These aneurysms may be situated in any of the sinuses but involve the right sinus most frequently they are usually the result of a congenital anomaly Occasionally these aneurysms are of syphilitic origin the result of atherosclerosis or a complication of subacute bacterial endocarditis particularly with bicuspid aortic valves They are more common in men

Aneurysms of the right sinus develop anteriorly and may cause erosions of the sternum and ribs They may cause a shadow to the right of the aorta and

occasionally are distinguished from aneurysms of the ascending portion of the aorta radiologically by the very small base which connects the shadow with the aorta Occasionally these aneurysms are so small that roentgen findings may be normal They develop often within the cardiac shadow These aneurysms may rupture into the right atrium or ventricle Aneurysms of the left sinus of Valsalva may be visible on the left side at the area of the pulmonic artery and may penetrate the left ventricle Rupture into the pericardial cavity and into the venae cavae also occurs The latter event causes the sudden appearance of cardiac murmurs over the base cyanosis and edema An aneurysm of the anterior sinus can cause pulmonary stenosis or tricuspid stenosis because of compression An aneurysm of the right lateral sinus can bulge into the right or left atrium

The murmurs in this lesion are continuous like those of patent ductus arteriosus Before perforation takes place the diagnosis is difficult

Symptoms

Aneurysms of the thoracic aorta were divided into aneurysms of symptoms and aneurysms of signs because according to location symptoms appear very early in one group while only objective signs without symptoms tend to occur in the other The former type occurs more often in the ascending aorta the latter in aneurysms of the transverse portion

The most common symptom is pain Often it is an angina on effort because stenosis of the coronary orifices is present Erosion of the ribs sternum and vertebra causes rest pain which may be excruciating particularly at night the site of this pain necessarily varies with the structures involved When pressure is exerted on nerve trunks intractable neuralgia appears Sometimes pain is referred and when noted in the left shoulder it is mistaken for an arthritis bursitis and the like

Second in frequency among the symptoms is dyspnea caused by pressure on the trachea or large bronchi It is usually of the inspiratory type similar to dyspnea caused by an obstruction of the upper air passages

If myocardial disease causes left ventricular failure paroxysmal nocturnal dyspnea occurs

Cough is common and represents the first and chief complaint in about 20 per cent of cases In many instances the history relates a series of colds the last one of which persisted Sometimes — with paralysis of the recurrent laryngeal nerve — the cough is brassy Often it is non productive Pressure of the aneurysm upon a large bronchus may however result in bronchostenosis and may cause distal bronchiectasis so that a profuse bronchorrhea and productive cough develop Secondary infections may alter the character of the sputum

Dysphonia (hoarseness) and dysphagia aid in locating the site of an aneurysm (transverse portion of the aorta) Dysphagia is not common since the esophagus is very mobile and easily escapes pressure in order for this symptom to appear, the aneurysm must bulge posteriorly just beneath the bifurcation of the

trachea Dysphagia usually does not occur in aneurysms of the lower descending thoracic aorta even if the aneurysm ultimately ruptures into the esophagus

Hemoptysis may occur early in the form of blood streaked sputum It may precede rupture of an aneurysm into a bronchus by several months

Palpitation is an infrequent symptom and too vague to aid in the diagnosis of aneurysm

In a relatively small number of cases the patient notices a mass bulging through the anterior chest wall Profuse perspiration due to pressure upon the sympathetic nerves herpes zoster and hiccough are sometimes early and non characteristic complaints If blood is aspirated into the lung and secondary infection develops fever and signs of bronchopneumonia may appear

Signs

Inspection may reveal edema of the face neck and upper extremities with *appropriately located aneurysms Sometimes congestion of the veins in the same* areas and a marked diffuse cyanosis also exist These signs are caused by compression of the superior vena cava Cyanosis is particularly marked when an aneurysm ruptures into the superior vena cava Compression of a single vein such as the right or left innominate vein may cause cyanosis limited to a circumscribed area

Sometimes a large tumor bulges on the upper right parasternal area through the sternum or to the left of it Classical expansile pulsations are not always present in this mass Secondary reactive inflammation of the tissue may cause a local increase of temperature in this area if as often happens the overlying skin is red and the aneurysm points like a boil the aneurysmal mass may be mistaken for an abscess an error by no means uncommon in the preroentgenologic era

Tracheal tug may be found in connection with aneurysms of the transverse portion of the aorta but it is by no means pathognomonic The neck veins may be markedly engorged A thrill or abnormal pulsation may be detected over the site of the aneurysm and abnormal dullness is also a common finding in this location A systolic murmur may be heard particularly in aneurysms of the ascending aorta this murmur is heard far to the right of the sternum Diastolic murmurs are also found without intrinsic involvement of the aortic valve owing to aortic regurgitation from distortion of the valvular ring Asymmetry in the pulsations of the carotid and brachial arteries and delayed pulses are often advanced as evidence of aneurysm It was pointed out however in the preceding chapter that aortitis without aneurysmal dilatation also produces this sign It is common in aneurysms since aortitis is always present when syphilis is provocative

Examination of the heart may yield normal findings despite a huge aneurysm This holds particularly for aneurysms at some distance above the supra valvular portion of the aorta for the aortic valves and coronary ostia are usually normal in these cases Pressure upon the azygos vein may cause marked right pleural effusion

Unilateral exophthalmus and mydriasis or enophthalmus with miosis (Horner s syndrome) appear with irritation or paralysis of the sympathetic nerves

Aneurysms may cause a paralysis of the right phrenic nerve with elevation and immobility of the right half of the diaphragm

Some of the symptoms and signs enumerated will lead to an x ray examination which usually provides positive evidence of an aneurysm It must be stressed however that the differential diagnosis from other mediastinal tumors may be difficult particularly when the clinician must rely upon physical signs alone Pulsations may be found in nonaneurysmal structures while a true aneurysm containing a large thrombus in its sac need not pulsate A small aneurysm that develops dorsad is especially likely to escape detection

In many cases the diagnosis of an aneurysm can be made only by an expert radiologist after prolonged observation Usually fluoroscopy is more satisfactory than roentgenograms The finding of calcium deposits in the tumor mass often facilitates the x ray diagnosis No fluoroscopy is complete without examination of the esophagus filled with a suspension of barium The trachea is often displaced to the left and a main bronchus may be visibly compressed Secondary pulmonic changes are discovered on x ray examination Careful study of the thoracic cage may reveal early evidence of bony erosion particularly of the vertebra in aneurysms of the descending aorta

The electrocardiogram is normal or — with stenosis or occlusion of the coronary ostia — altered as in other forms of coronary disease

Differential Diagnosis

While easy or obvious in some cases the diagnosis of the lesion presents *great difficulties in others The clinical picture is extremely variegated* Confusion with other conditions was frequent before the roentgenologic era and occurs even today

Rheumatism arthritis asthma and chronic bronchitis are the most common diagnostic errors in these cases The lesion is also confused with bronchogenic carcinoma from which it can sometimes be differentiated only with great difficulty Angiocardiography may be necessary A carcinoma of the esophagus may be wrongly diagnosed if the aneurysm is too small to be seen but causes esophageal symptoms It occasionally happens that patients are treated for a simple laryngitis if they complain only of hoarseness

Course of the Disease and Mode of Death

Aneurysms are a severe affliction and the prognosis is poor Patients with huge aneurysms may lead an active life for years but such cases are exceptional Statistics on the duration of the disease are limited only to the estimated duration after the appearance of symptoms usually the lesion has existed for a much longer time In the majority of cases death occurs within two years after the onset of symptoms but patients are known whose aneurysms were observed for *20 or 30 years (Boyd) Instances of healing of the aneurysm by* spontaneous obliteration of the sac through organization of the thrombus are so rare that they are listed among the curiosities of medicine

About half of the aneurysms of the thoracic aorta terminate by rupture. Most of the remaining cases die from the mechanical effects of pressure on various organs. Only a small percentage of patients die from unrelated disease.

External rupture of the aneurysm is uncommon even when there is a large protruding mass. In a series of 1197 cases of rupture of a thoracic aneurysm external rupture occurred only 61 times (Boyd). In aneurysms of the ascending aorta, intrapericardial rupture occurred in one third; next in frequency was rupture into the left pleura, the left bronchus, and into the esophagus. Rupture may also occur into the right pleura, right main bronchus, the pulmonary artery or the superior vena cava (causing a sudden and marked increase of cyanosis). Aneurysms of the arc often rupture into the trachea, a bronchus or the esophagus. Aneurysms of the descending aorta usually rupture into the left pleural cavity, left bronchus, or esophagus. For a more detailed description of all possibilities reference should be made to reviews of the literature on this subjects.

Rupture into the pulmonary artery causes sudden collapse, shock, progressive dyspnea, a constant murmur and thrill in systole and diastole in the second or third left intercostal space parasternally, pulsus celer and right ventricular failure.

Rupture into the superior vena cava causes a similar thrill and murmur to the right of the sternum and signs of superior vena cava obstruction.

Rupture through a serous surface (pleura, pericardium) occurs without warning and causes sudden death. Rupture through a mucous membrane (esophagus, trachea) may give warning in the form of slow bleeding or oozing. Sometimes bleeding, even if rather profuse, is not immediately fatal, but a lethal hemorrhage may occur a few days afterward.

ANEURYSMS IN OTHER LOCATIONS

Aneurysm of the Innominate Artery

These aneurysms develop near the right sternoclavicular articulation. Pain and throbbing in the neck constitute the chief symptoms. The aneurysmal sac is usually palpable and a thrill is found. The right jugular vein may be distended and edema of the right side of the face may appear. The right carotid and right *brachial pulse are smaller.*

It has been pointed out that elongation of the aorta with high position of the innominate and right subclavian artery and kinking of the carotid artery are often confused with these aneurysms.

Aneurysm of the Pulmonary Artery

This is a rare lesion. In two thirds of the observed cases, the common trunk of the pulmonary artery was affected (Boyd and McGavack). In nearly one half of the cases reported, one or more congenital abnormalities, such as patent ductus arteriosus, stenosis of the pulmonary orifice, and atrial septal defects, were present. Syphilis is an etiologic factor in the acquired variety.

arteriosclerotic mycotic and traumatic aneurysms though well known are less common

There are no characteristic symptoms Palpitation is present early while cyanosis and dyspnea appear later The diagnosis can be made if a pulsation and a systolic thrill are found on the left side parasternally in the area of the second or third intercostal spaces with a loud systolic murmur, and if x ray examination shows a marked and circumscribed dilatation of the pulmonary artery

Even with x ray examination differentiation from an aneurysm of the aorta is sometimes impossible since aneurysms of the ascending aorta may develop on the right side and simulate dilatation of the pulmonary artery The presence of hilar pulsation may help in the differentiation

Undoubtedly many patients in whom the diagnosis of aneurysm of the pulmonary artery has been made without postmortem confirmation in reality had an atrial septal defect

Aneurysms of the Abdominal Aorta

These aneurysms are about as common as those of the descending portion of the thoracic aorta They appear however in an older age group that is in patients over 50 Arteriosclerosis is the most common cause Syphilis is not rarely responsible for these aneurysms whereas other infections such as tuberculosis are exceptional etiologic factors In one series (Mills and Horton) evidence of syphilis was found in 8 8 per cent while the incidence of syphilis in another series was placed as high as 58 per cent (Scott) In abdominal aneurysms lesions are multiple in 18 to 20 per cent of the cases Trauma is rarely responsible

The aneurysmal sac is often located in the anterior aortic wall just below the diaphragm particularly in aneurysms of syphilitic origin Arteriosclerotic aneurysms lie at the celiac axis for the most part

The chief symptom is abdominal pain which may be overwhelming and which may appear in paroxysms lasting minutes or hours The pain is throbbing and appears particularly at night or after a meal The pain may spread to the thigh the scrotum or the labia as in a kidney stone In addition to the pain nausea and vomiting often occur Obstipation and meteorism are common Reactive inflammation of the surrounding tissue may cause peritoneal irritation The aneurysm may compress the stomach a part of the intestines or a ureter causing corresponding symptoms Erosion of the vertebrae and compression of the spinal cord may produce hemiparesis or paraplegia

A pulsating tumor the size of an orange or even larger is often found on palpation It must be emphasized that the mere fact a tumor pulsates does not by itself confirm the diagnosis The pulsating mass must be wider than the normal aorta Evidence of expansile pulsation in all directions is necessary because the pulsation may be transmitted The tumor is often tender on palpation Occasionally a murmur is heard and a thrill is felt over the aneurysm

Flat x ray plates of the abdomen are a great diagnostic help The aneurysm is often outlined by the deposits of calcium present in the aneurysmal wall Erosion of the vertebrae is occasionally noted in lateral plates With tomography one may find a soft tissue mass

The duration of the lesion depends upon its size and location Usually rupture takes place in six to twelve months after the appearance of symptoms but cases of much longer duration are known In one group of statistics 20 per cent of abdominal aneurysms without complaints survived for five years

At times the rupture occurs into the duodenum or the abdominal cavity Not rarely the rupture is retroperitoneal Patients may survive this type of rupture for a few days often in a deepening coma In not a few patients the course of the disease is interrupted by episodes simulating peritonism or ileus which subside after several days

One must make sure not to confuse an abdominal aneurysm with a strongly pulsating normal abdominal aorta which is easily felt in patients with enteroptosis

Aneurysms of Peripheral Arteries

The majority of these aneurysms are of embolic mycotic origin The etiology is usually a bacteremia in the course of subacute bacterial endocarditis chronic empyema or osteomyelitis The infected emboli lodge in the vasa vasorum Small mycotic aneurysms that occur in the aorta are usually not diagnosed clinically they are more often found in the peripheral arteries Rupture is a common event before these aneurysms reach large dimensions Nearly one third of these patients are under 20 years of age The lesion is often overlooked if it occurs in a peripheral artery it is often confused with phlebitis

Erosion of an artery by an extrinsic process leads to the formation of an aneurysm in rare cases

Syphilitic aneurysms also occur at times in peripheral arteries Thus aneurysm of the popliteal artery was rather common and was perhaps next in frequency to aneurysm of the aorta We observed a syphilitic aneurysm in the radial artery

Congenital aneurysms especially common in the cerebral arteries stem from malformations of the arterial wall They are most often situated at the circle of Willis They may cause sudden hemiplegia with xanthochromic spinal fluid and severe occipital headache These accidents need not occur until adult life is reached Some patients are over 40 years of age when symptoms appear The dramatic picture of a subarachnoid hemorrhage may also be the result of a rupture of a congenital cerebral aneurysm

Similar congenital miliary aneurysms have been observed in the coronary arteries otherwise an uncommon site of aneurysm coronary artery aneurysm may be due to periarteritis nodosa In unusual instances it follows stab wounds Congenital aneurysms of the coronary arteries are often multiple sometimes rupturing or becoming thrombosed

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DISSECTION OF THE AORTA AND CYSTIC MEDIONECROSIS

Separation of the coats of the aorta or dissecting aneurysm was observed by Morgagni and was well known to Laennec In the past the diagnosis was made only at postmortem examination The number of cases in which correct clinical diagnosis is made has increased since Shennan s excellent monograph was published The term dissection of the aorta is preferable to dissecting aneurysm

Incidence

It has been estimated that the lesion occurs once in about 400 necropsies (Sailer) or once in 480 autopsies of patients over 20 (Gouley and Anderson) In another series of 3129 autopsies 12 dissecting aneurysms were found There fore the condition is not extremely rare While it has been seen in an infant of 14 months and in a 100 year old woman it is most common in males after the age of 60 It is more common in hypertensive patients than in those with normal pressure although this has been denied by some

In young women dissection of the aorta has been observed particularly during pregnancy and in the presence of coarctation of the aorta It was observed in a 34 year old woman and her 14 year old son Eighty per cent of the patients are beyond 60 years of age and 65 per cent are males

Pathology

Hemorrhage between the layers of the aorta may occasionally follow trauma erosion of the aorta by an abscess tumor or arteriosclerotic changes (atherom atous ulcer) but the most common cause is medionecrosis cystica of the aorta (Erdheim Gsell)

This lesion is recognized as the outstanding cause of spontaneous rupture of the aorta and of the dissecting aneurysm It is usually limited to the ascending aorta Small areas of degeneration develop in the inner part of the media without any sign of inflammation According to some investigators the change involves primarily the elastic fibers and the connective tissue according to others the muscle fibers are affected first Later an over production of mucoid material and the formation of cysts may be seen These focal mucoid changes and necroses in the aorta were described before but their relation to the dissecting aneurysm remained unknown until the publication of more recent pathologic investigations (Erdheim) The absence of evidence of inflammation distinguishes the lesion from aortitis while the localization in the media with the intima remaining intact separates it from atherosclerosis On gross examination the lesion often resembles syphilitic aortitis

The etiology of the process is unknown It possesses some similarity to experimental necrosis of the media of the aorta seen in rabbits following injections of epinephrine Therefore excessive strain and stress have been alleged as causative Others think that infectious di eases such as scarlet fever or typhoid fever are responsible Marked damage of the arteries in infectious diseases has

is presented when the mesenteric arteries are involved or the dissecting aneurysm ruptures into the ... en

Evidence ... of disturbed blood supply in the lower extremities may be found if the ... and their branches are affected. A bruit and thrill may appear ... artery (Logue). The local picture may resemble that of a peripheral ... or thrombosis. In addition to the clinical findings already ... in the pleural cavity, vomiting, nausea, a ... rhythm.

Examination ... heart often reveals a systolic and a diastolic murmur. The latter ... feature in patients with a typical evolution of the syndrome ... displacement of the aortic valves when the dissection involves the ... an event which occurs in more than 70 per cent of the cases.

Rupture ... causes aphonia and dysphagia. Hemoptysis is common ... explained.

Roentgen ... examinations have been made repeatedly but naturally only in the patients who survive for a while. Widening of the aortic knob and ... contour in the ... and abnormal shadows along the large vessels of the cardiac base may be seen. Sometimes these shadows pulsate. X-ray examination ... helps to establish the diagnosis.

Differential Diagnosis

The picture of the condition is protean and presents great diagnostic difficulties; the number of cases in which the diagnosis is reached ante mortem is increasing but still is not large.

The excruciating pain presented by patients is usually confused with the pain of coronary occlusion and myocardial infarction. It is pointed out by various authors that the pain in dissecting aneurysms is more knifelike than compressive or vicelike; the wandering of the pain down the back may help in the differentiation but this symptom is often missing or late in appearance.

The elevated temperature, leukocytosis, pericardial involvement, electrocardiographic changes and fall of blood pressure are found in both conditions. The blood pressure, however, usually remains high in dissecting aneurysm. This fact, together with the appearance of a diastolic aortic murmur and the absence of pulsation in one carotid or brachial artery, will help in the diagnosis. The absence of electrocardiographic changes in coronary occlusion is rare; the presence of changes that indicate a myocardial infarction in dissecting aneurysms is unusual. The differentiation may be easier if the patient survives for several hours, but often is impossible at the onset of symptoms. Since the immediate treatment consists of an injection of morphine in both conditions, nothing is lost from a therapeutic standpoint. The differentiation is, however, important for prognosis.

The possibility of confusion with pericardial involvement was already mentioned. In one series of 12 cases the rupture took place into the pericardium in 7 instances (Logue). In chronic dissections ... in patients surviving for some

Dissection of the Aorta and Cystic Medionecrosis

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been described (Wiesel) The frequent occurrence of vascular lesions in rheumatic fever has been pointed out before but these lesions are of a different type Both the excessive use of tobacco and the occasional presence of syphilis were considered etiologic factors Toxins of unknown character are also supposed to be causal

Medionecrosis is common It has been seen in 95 cases among 210 routine necropsies (Rottino) The incidence is higher with increasing age and with increasing blood pressure

The vasa vasorum in the aorta suffer in this process It seems probable that rupture of the vasa vasorum leads to a hemorrhage between the layers of the media If this hemorrhage extends it may lead to complete rupture of the weakened aortic wall More often the tears run up and down the aorta causing the dissection The intimal wear is thus a point of emergence and not as it was believed for many years a point of entrance and the beginning of the dissection (Sailer) In favor of this conception is the fact that dissecting aneurysms have been seen in which the intima was intact Gore and Seiwert report 23 instances in which there was no intimal break The tear has two points of predilection explained easily by the anatomic situation One is just above the aortic valves that is 2 to 4 cm above the sinus of Valsalva the other is in the area of the aortic isthmus In coarctation of the aorta dissection is not rare The tear in the ascending aorta is usually transverse

The separation of tissue of the media (which takes place chiefly in the outer layers) may proceed centrally toward the heart and occlude the coronary arteries Usually the dissection burrows peripherally and all arterial branches originating from the aorta can be involved At first they remain connected with the main stem of the aorta by the thin intima alone but soon the vessel is occluded and severed at its origin This may happen to the innominate artery the left carotid artery and left subclavian artery to the intercostal and lumbar arteries the renal and mesenteric arteries and so forth The dissection may proceed down to the femoral and even to the popliteal vessels In a 15 year old boy the dissection reached the posterior tibial artery in one side and the popliteal artery on the other There was also some dissection of the pulmonary artery (Gardner et al) Since the dissection rarely involves the whole circumference of the wall of the aorta not all aortic vessels are involved during the progress of the lesion

The dissection may re enter the lumen of the aorta at any point or rupture into the surrounding area If the blood re enters the aorta the patient occasionally survives and an endothelial lining forms in the new path These patients have a double barrelled aorta If the entire circumference of the aorta is involved in the whole path of the aneurysm the inner part of the aorta may be carried down toward the periphery as an embolus If the dissection breaks outward — a common event — severe hemorrhage may occur into the pericardium the mediastinum the pleura or abdomen resulting in sudden death

Incomplete rupture of the aorta (as well as complete rupture) has a similar underlying pathology Incomplete rupture may also cause the sudden appearance

of an aortic diastolic murmur (Peery) Of great interest is the production of the lesion in rats fed lathyrus odoratus (sweet pea seeds) (Bachhuber and Lalich) or aminonitriles (Wawzonek et al) The toxic substance is beta aminopropionitrile (Bean and Ponsetti) Kyphoscoliosis and hernias may coexist showing a tendency to a connective tissue injury

Symptoms and Signs

The most outstanding symptom is the sudden and overwhelming pain which strikes the patient with full force and without premonitory symptoms often beginning during physical work Some believe that a sudden rise of blood pressure may be an initiating factor responsible for dissection The pain is knifelike and often spreads to the shoulder or is felt only between the scapula Sometimes it wanders down with the progress of the dissection Occasionally it extends into the right or left arm At times it is intermittent sometimes it is mild or even completely absent Baer et al missed the pain in 20 out of 44 cases Usually there is no compressive sensation as exists in anginal pain due to myocardial infarction If the pain is felt only in the back or in the abdomen confusion with other lesions may arise In general the location of the pain depends upon the site of the aortic lesion

Vomiting and nausea as well as profound shock occur often the clammy skin is covered with sweat Dizziness appears and the patient may lose consciousness this happens particularly when one carotid artery is involved and suddenly becomes occluded Convulsions occur as well as disorientation and dyspnea

The blood pressure may fall the temperature rise and *there is* a marked leukocytosis which may reach 30 000 white cells with more than 90 per cent polymorphonuclear cells

Most of the other symptoms and signs naturally depend to a great extent on the location and spread of the dissection and the vessels involved

Dissection toward the heart may cause occlusion of coronary arteries with myocardial infarction and all its consequences The electrocardiogram then shows the changes expected in a myocardial infarction and a pericardial friction rub may appear Rupture of the dissection is particularly common and may cause the clinical syndrome of cardiac tamponade it soon proves fatal

The innominate artery may escape but the left subclavian and left carotid artery are often compressed or occluded This may lead to hemiplegia hemiparesis or paralysis of one limb and other neurologic phenomena The left arm may become pale and bloodless and the pulsation of its arteries disappears

Dissection of the intercostal and lumbar arteries may lead not only to pain that gradually wanders down the back but also to such segmental neurologic findings as hyperesthesia or anesthesia Paraplegia is also observed The dissection of the intercostal arteries and occlusion of branches supplying the anterior aspect of the spinal cord may account for the overwhelming weakness of the legs a common and major complaint

Involvement of the renal arteries leads to renal infarction renal hemorrhage anuria and uremia Bloody stools may appear and the picture of an acute abdomen

is presented when the mesenteric arteries are involved or the dissecting aneurysm ruptures into the abdomen

Evidence of a disturbed blood supply in the lower extremities may be found if the femoral arteries and their branches are affected A bruit and thrill may appear over the femoral artery (Logue) The local picture may resemble that of a peripheral arterial embolism or thrombosis In addition to the clinical findings already mentioned are blood in the pleural cavity vomiting nausea and gallop rhythm

Examination of the heart often reveals a systolic and a diastolic murmur The latter a characteristic feature in patients with a typical evolution of the syndrome results from displacement of the aortic valves when the dissection involves the ascending aorta an event which occurs in more than 70 per cent of the cases

Rupture into the mediastinum causes aphonia and dysphagia Hemoptysis is common and not well explained

Roentgenologic examinations have been made repeatedly but naturally only in those patients who survive for a while Widening of the aortic knob a double contour in this area and abnormal shadows along the large vessels of the cardiac base may be seen Sometimes these shadows pulsate X ray examination rarely helps to establish the diagnosis

Differential Diagnosis

The picture of the condition is protean and presents great diagnostic difficulties the number of cases in which the diagnosis is reached ante mortem is increasing but still is not large

The excruciating pain presented by patients is usually confused with the pain of coronary occlusion and myocardial infarction It is pointed out by various authors that the pain in dissecting aneurysms is more knifelike than compressive or viselike the wandering of the pain down the back may help in the differentiation but this symptom is often missing or late in appearance

The elevated temperature leukocytosis pericardial involvement electrocardiographic changes and fall of blood pressure are found in both conditions The blood pressure however usually remains high in dissecting aneurysm This fact together with the appearance of a diastolic aortic murmur and the absence of pulsation in one carotid or brachial artery will help in the diagnosis The absence of electrocardiographic changes in coronary occlusion is rare the presence of changes that indicate a myocardial infarction in dissecting aneurysms is unusual The differentiation may be easier if the patient survives for several hours but often is impossible at the onset of symptoms Since the immediate treatment consists of an injection of morphine in both conditions nothing is lost from a therapeutic standpoint The differentiation is however important for prognosis

The possibility of confusion with pericardial involvement was already mentioned In one series of 12 cases the rupture took place into the pericardium in 7 instances (Logue) In chronic dissections i e in patients surviving for some

time the presence of a Corrigan pulse an increased pulse pressure and a diastolic aortic murmur in the second right intercostal space parasternally may cause confusion with syphilitic aortic regurgitation

For obvious reasons the disorder may be mistaken for a cerebral accident a pleural effusion renal disease an abdominal lesion and particularly a surgical emergency

The differentiation is especially difficult if there is no pain or if the pain is not felt within the chest If patients complain only of weakness in the legs or abdominal colic with diarrhea or pain in the back the diagnosis will be possible only for those who are thoroughly familiar with the picture and think of it The *disappearance of peripheral pulses the wandering of the pain down along the aorta* and the appearance of a diastolic aortic murmur are the best diagnostic signs

Prognosis

The prognosis is very bad Only 7 per cent of Shennan s patients lived for 1 to 5 weeks Healed cases usually with a double barrelled aorta are rare but survival for several years is observed (Hoskin and Gardner) In some of these patients no history could be elicited pointing to the date of dissection Apparently it proceeded without pain and did not make the patient sufficiently ill to require rest in bed In most patients even when they survive for a time the dissection resumes its course and causes perforation and death

Treatment

As pointed out before morphine is indicated to relieve the pain Complete rest is advised and enforced with the administration of barbiturates and other sedatives Oxygen has been repeatedly recommended but its value is dubious An operation designed to relieve pressure from a compressed femoral artery was attempted (Gurin et al) and an attempt was made apparently successful to operate on some patients in the hope of diverting the blood and causing its re entry into the aorta (de Bakey et al) It is in this way that self healing occurs in aortic dissection — spontaneous re entry

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Chapter 25

Atheroma of the Aorta and Atherosclerosis of Smaller Arteries

ARTERIOSCLEROSIS APPEARS in three main forms as atherosclerosis in the aorta and many large arteries as the harmless media sclerosis and as arteriolosclerosis of the small arterioles in hypertension

Atheroma of the Aorta This lesion begins early in childhood it becomes well developed in the fifth decade and varies only in degree in different individuals It is not however a physiologic phenomenon As in other forms of atherosclerosis the etiology is unknown although a disturbance of lipid metabolism is frequently assumed In this purely degenerative process lipid infiltration degeneration with necrosis and intimal proliferation are combined secondary calcification takes place The aorta or any involved artery becomes elongated and tortuous If an atheromatous placque ruptures debris is sent toward the periphery and causes embolism Sometimes an aneurysm forms an event observed particularly in the abdominal aorta

Pure atheroma causes no symptoms and the condition may progress very gradually without any important disturbance of the circulation Often it is an incidental finding

With advancing age the elasticity of the aorta diminishes The normal aorta has a storage function It receives the output from the left ventricle and moves it slowly toward the periphery with the aid of its elastic and smooth muscle fibers In this way the blood flow which receives rhythmic impulses by the contraction of the left ventricle becomes steadier The ascending aorta acts as a compression chamber With increasing age diminished elasticity of the aorta and athero sclerosis this function of the ascending aorta disappears and with it the systolic blood pressure rises while the diastolic tends to fall The size and shape of the heart remains normal A systolic murmur is audible over the aorta and is often trans mitted to the apex as are all systolic aortic murmurs In elderly patients with emphysema the basal murmur at the second right interspace disappears while the systolic murmur over the apex remains and may cause confusion with other murmurs Often the systolic apical murmur is created by a sclerosis of the mitral valves while the systolic aortic and apical murmurs may be caused by athero sclerosis of the aortic valves The systolic aortic murmur is often midsystolic that is sharply separated from the first sound by an interval It may appear at the end of systole (figure 91) The second aortic sound is accentuated and may even be metallic or ringing as in aortitis

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Atherosclerosis of the larger renal arteries may cause contraction (athero sclerotic contracted kidney) and scars but it rarely disturbs renal function It is asymptomatic Albuminuria is a common sign

Aneurysms due to atherosclerosis have been discussed in the preceding chapter

Therapy No treatment is known A well regulated life may add to the patient s comfort and lessen the opportunity for various vascular accidents The individual should adapt himself to a slow pace — avoidance of excesses of food and drink elimination of sudden strains either physical or mental and so on The amount of fat in the food should be small Eggs cream butter and margerine are forbidden

The time honored prescription of iodides is still widely used in some countries As a rule such drugs are harmless and often beneficial especially in cerebral vascular sclerosis Since arterial changes following the feeding of cholesterol to rabbits can be prevented by the administration of iodides the empirical use of this drug may have some rationale

Chapter 26

The Cardiovascular Neuroses and Neurocirculatory Asthenia

IT IS DOUBTFUL whether a sharp line of demarcation can be drawn between cardiovascular neurosis and neurocirculatory asthenia We prefer to discuss the two conditions as separate entities even though there are many strong arguments against the appropriateness of such a division

CARDIAC NEUROSIS

The cardiac neuroses are among the problems rarely encountered in the hospital but often met in private practice An extremely variegated picture is involved Recognition of the condition is often difficult and treatment requires much experience tact and knowledge of human nature Undoubtedly many cases were formerly included which did not belong in this group In old treatises on this subject extrasystoles paroxysmal tachycardias and even angina pectoris were diagnosed and discussed as cardiac neuroses Until recently several disturbances found in women and connected with ovarian dysfunction that are now *quickly and successfully treated with estrogens were attributed to* a neurosis

The complaints are diverse Palpitation dyspnea and precordial pain stand in the foreground as they do in many organic heart diseases The experienced physician however will discover by a few questions that the palpitation and pain are independent of effort they appear on excitement or without any external reason and they may last for hours The respiration may be completely irregular if dyspnea is present it may be purely subjective and without discernible change of rate or depth of the respiration Insomnia inability to concentrate or work a tendency to perspire readily anxiety and restlessness supplement the picture Outwardly these patients may seem very quiet many of them do not present the picture designated by laymen nervousness The pain rarely radiates to the arm and it is equally unusual for it to be retrosternal More often it is inframammary or near the apex

The signs and differential diagnosis will be discussed in connection with neurocirculatory asthenia since in this condition similar complaints are offered and the same signs are found

Patients with cardiac neuroses with any neurosis for that matter are *patients* and must be treated as such They suffer from their distress and their families suffer *with them For this reason it is entirely wrong* to tell the patient that his complaints are only imaginary An unpleasant situation is created

when the patient is told there is nothing wrong with him that all complaints are purely nervous and the family is informed by the physician that the patient is hysterical It is much better to explain to the patient and to his relatives in keeping with the facts that no *organic* heart disease is present the disturbance is not dangerous nor will it lead to complications rather an alteration of the cardiac nerves and of the nervous regulation of the heart is present which merits careful consideration and requires careful treatment however *it is definitely curable and will have no consequences* Many neuroses vanish as soon as the relatives adopt a different attitude toward the patient upon the advice of the physician

In treating this type of patient it is not advisable to rely chiefly on medicinal therapy Bromides chloral hydrate preparations of valerian and the modern tranquilizers are excellent supportive agents but they have little value by themselves Psychotherapy is much more important For this purpose much experience is necessary but special training is not indispensible Careful interrogation and detailed inquiry into the symptoms should establish a close contact between physician and patient Often one will succeed in discovering domestic strife professional dissension or material or sexual preoccupations as the source of initiating factors in the neurosis Corresponding counsel explanation and encouragement will aid remarkably Hardly ever does one have the satisfaction of having helped so much and hardly ever does one acquire so thankful a patient as in this oft neglected group

NEUROCIRCULATORY ASTHENIA

This condition is also known as Da Costa s syndrome irritable heart soldier s heart and autonomic imbalance As indicated earlier we are dealing here with a syndrome that cannot be distinguished from a cardiac neurosis

Occurrence Frequency

While the disorder is occasionally encountered in times of peace it seems to be particularly prevalent during wartime and when people are under stress and strain Da Costa originally described the condition during the Civil War About 44 000 cases became pensioners because of this disease in Great Britain during the First World War (Parkinson) Out of every 10 patients admitted to a hospital allocated for the care of cardiac patients in the period 1914—1918 nine suffered from neurocirculatory asthenia or D A H (disordered action of the heart as it was called by the British Army) (Lewis) There is evidence to show that more than 1 5 per cent of the rejections by draft boards in the United States during the recent war were due to neurocirculatory asthenia In the Second World War one out of every ten soldiers admitted to hospitals for cardiac complaints had neurocirculatory asthenia

Naturally men are more often affected in time of war when the ratio seems to be 3 to 2 in favor of males This figure may be reversed in times of peace About 30 per cent of the patients are engaged in hard labor (Hill and Dewar)

Symptoms

Fatigue A regular and outstanding symptom is great fatigue Characteristically the patients complain of it when awakening in the morning after a long sound sleep This profound exhaustion makes the patient dread any activity In mild cases as in all neurotics the feeling of fatigue may vanish during the day If the patient is active he tires easily

Dyspnea This is a common complaint It is described as the sensation as if the breath would not go through and has been discussed in the first chapter The hyperventilation syndrome is common

Pain Sometimes stabbing pain is felt in the inframammary region or more rarely behind the sternum It may radiate to the left arm and thus may be very misleading Like the pain in other cardiac neuroses it bears no relation to effort it does not come during the excitement but hours afterward The area over the left breast or the apex is sore to touch This symptom is very difficult to explain The pain may also be dull

Palpitation This complaint is also very common and of the same type as that discussed in the other neuroses Like the dyspnea and pain it occurs often at rest and is particularly annoying The cardiac rate may be slow Many patients are distressed by palpitation and precordial pain when lying on the left side Since the same complaint occurs in about 30 per cent of normal people it is usually easy to reassure the patient as to its benign nature

Wood found dyspnea in 93 per cent fatigue in 88 per cent and sweating in 80 per cent of the subjects Nervousness was noted in 79 per cent and dizziness as well as pain in 78 per cent

Additional Complaints Many patients tend to perspire profusely This is very annoying if the hands are affected for these parts feel cold and clammy Some patients perspire on the least mental or physical effort Headache dizziness trembling and irritability are added complaints Some patients also mention blurring of vision numbness of the extremities loss of memory and inability to reach decisions

Signs

The hands are often blue (stagnant anoxemia) there is hyperpnea and the knee jerks are exaggerated

Cardiac hypermotility is easily found on palpation of the precordial area The heart beat is often accelerated and rates exceeding 120 at rest may be found usually the heart slows during sleep Physiologic systolic murmurs may be heard The first heart sound is loud at the apex Sometimes the blood pressure is elevated to 150/90 mm Hg or more (anxiety hypertension) presumably as the result of cardiac hypermotility The diastolic blood pressure may be normal even if the systolic pressure is markedly elevated (Hill and DeWar) The heart is always normal in size and shape if no unrelated complications exist Often x ray examination discloses a moderately dilated aorta This is a dynamic dilatation as in hyperthyroidism and the hypermotility of the left ventricle which expel it

stroke volume with greater force into the ascending aorta is largely responsible for this finding

Electrocardiographic findings have been described but they are equivocal and do not aid in the diagnosis

Many of these patients have a spastic colon and gastric hyperacidity A mild elevation of temperature is common and may be misleading

Etiology

The cause of the syndrome is unknown Stress is often a precipitating factor In some cases great nervous strain physical overexertion an exhausting illness or an infectious disease antedate the onset of neurocirculatory asthenia Emotional conflicts play a great role and explain the increased frequency of this syndrome in wartime It is found not only in cowards but also in men with a keen sense of duty Heredity is important for the family history is positive in approximately 50 per cent of the occurrence of psychiatric cases The imbalance of the autonomic nervous system is attributed by some to a central disorder The hypothalamic region has been suspected as the possible site of the lesion

According to Wood the symptoms resemble those of fear more than those of effort The mechanism is one of central stimulation The symptoms are the same as those observed in situations provoking anxiety and alarm It is an emotional reaction pattern peculiar to psychopathic personalities and subjects with almost any type of psychoneurosis

Prognosis

The syndrome is never dangerous to life and there are no serious complications Temporarily hyperventilation may cause tetany and even a condition like shock (hyperventilation syndrome) The extreme prostration may incapacitate the patient so much that months are spent in bed The outlook in respect to the duration of the syndrome depends upon many factors not the least of which is the correct management of the patient In the First World War 20 per cent of the patients recovered sufficiently for re entrance into general service 20 per cent were permanently unfit and the rest improved sufficiently to do light work The outlook for very advanced (stretcher) cases is poor A follow up study of more than 600 cases of the war of 1914—1918 revealed that 15 3 per cent of the patients recovered entirely 56 2 per cent remained stationary 3 2 per cent became worse and the rest improved (Grant) The death rate in these cases was no greater than in the general population but a remarkable number (22 cases) developed pulmonary tuberculosis

Differential Diagnosis

The distinction between neurocirculatory asthenia or cardiac neurosis and organic disease or extracardiac lesions sometimes offers great difficulties

A history of dyspnea a loud first sound over the apex and a systolic apical murmur may lead to the diagnosis of a rheumatic mitral disease It is easy to

rule out an advanced mitral lesion by x ray examination in the right oblique position this rule is not valid for early cases of mitral stenosis because in this instance the left atrium need not be enlarged

The increase of blood pressure the systolic murmur and the history of pain with typical radiation may suggest coronary disease with angina pectoris The differentiation between neurotic pain and atypical angina pectoris in coronary disease may meet with unsurmountable obstacles with the result that the final decision may have to be deferred for a while The appearance of pain with no relation to effort or excitement its prolonged duration or short stabbing character and the absence of any favorable response to nitroglycerin (therapeutic test) speak in favor of the neurotic pain and help in the differentiation It is noteworthy on the other hand that in coronary sclerosis a few hours or days before the full picture of coronary occlusion and myocardial infarction appears the attacks may also be atypical and may not even respond to nitroglycerin

In view of the paucity of objective signs malingering is not easily excluded

Hyperthyroidism is often suggested in these cases by virtue of the tremor the profuse perspiration the tachycardia and the cardiac hypermotility In neurocirculatory asthenia however there are no eye symptoms the basal metabolic rate is normal and the tachycardia disappears during sleep In both conditions the hands are moist but they are cold in neurocirculatory asthenia and warm in hyperthyroidism The condition may also be confused with brucellosis

The presence of slight temperature loss of weight and tachycardia may seem to indicate a beginning pulmonary tuberculosis Therefore a complete physical examination should be followed by roentgen examination of the lungs In this connection it should be recalled that temperatures of organic origin such as those of rheumatic fever tuberculosis and so forth are easily abolished by small doses (2 Gm daily) of aminopyrine (Pyramidon) The fever found in neurocirculatory asthenia or in hyperthyroidism is not modified by this drug but is lowered by opium derivatives

Experience during the recent war in particular has taught the importance of ruling out an early hypertension in these cases Blood pressures exceeding 150/90 mm Hg are common in neurocirculatory asthenia and only careful observation and the presence of hypertensive heart disease in one or both parents may permit the differentiation

Therapy

Not much help can be expected from drugs Small doses of chloral hydrate bromides or phenobarbital are useful and benzedrine has been recommended for the asthenia Tranquilizing agents seem to help Vitamins are given a tonics However medication prescribed is only for symptomatic treatment and does not cure the patient The less attention paid to the pulse rate and the heart once the diagnosis is established the easier it is to handle the situation

Of primary importance is psychotherapy with firm reassurance of the patient Fear should be removed if possible and the patient should be taught to readjust himself to his environment He should be taught to have a more philosophical attitude towards situations at home and in business Sometimes the help of a psychiatrist is needed but often the patient resists this advice for obvious reasons Much patience and much listening to the patient s complaints are necessary One often finds difficult life situations that cause emotional tension and here advice may be helpful The word neurosis is avoided The physician should never forget that a cardiac neurosis may have been initiated by an injudicious statement of a colleague Explanation of the nonorganic nature of the complaints does more good than mere reassurance Graduated exercises were in vogue for patients of this group during the First World War

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Chapter 27

Cardiac Diseases and Pregnancy

THE MOST COMMON HEART DISEASES of women in the childbearing age are rheumatic fever and hypertension. Congenital heart disease, cor pulmonale (particularly in kyphoscoliosis) or arteriosclerotic heart disease are less frequent.

The attitude of different physicians in many problems arising in these patients depends upon their background, experience and education. Thus the gynecologist invariably speaks of pregnancy complicated by cardiac involvement, while the cardiologist talks about a cardiac disease complicated by pregnancy.

The responsibility a physician assumes in every decision is very great. He should never rely upon statistical results alone but should individualize each case on its own merits after thorough examination and observation. Statistics, however, as compiled in two monographs (Jones; Hamilton and Thomson) make the task easier and offer help in making the final decision. Unfortunately, the attitude of many physicians confronted with the problems we are about to discuss often depends neither upon the experiences of others nor the known facts, but upon single recent personal observations.

Incidence. The incidence of rheumatic fever in pregnant women varies in different parts of the world but some idea of the importance of the problem can be obtained from the following figures.

In New England, the incidence of rheumatic heart disease among pregnant women is 1.5 per cent (Kellogg). In the Boston Lying In Hospital 1.7 per cent of pregnant women were cardiacs (Hamilton and Thomson). In New York rheumatic heart disease was found in 2.6 per cent of pregnancies, while in Great Britain 0.25 per cent of cardiac cases were detected among 20,306 deliveries (Donovan). Similar figures were recently obtained by Abramson and Tenney despite the lower incidence of rheumatic fever in the last few years. In all hospital statistics the number of cardiac patients is naturally higher than in the general population, since women with heart disease fortunately are referred to hospitals for observation and delivery in ever increasing numbers.

Heart disease ranks among the five most important causes of maternal death. It accounts for about 7 per cent of all fatalities and claims close to 1000 pregnant women a year in the United States.

Pathophysiology. Pregnancy increases the load for the heart, diminishes its reserve power and may cause decompensation in patients with organic heart disease. The work of labor magnifies this strain.

The circulating blood volume increases during pregnancy by 45 per cent beginning early in pregnancy and gradually reaching a maximum in the ninth lunar month There is a progressive increase in the plasma and total volume by 30 to 50 per cent A definite decrease occurs in the tenth lunar month and after delivery The red cell count hemoglobin percentage and hematocrit increase Because of the relatively greater increase of the plasma a relative anemia appears to be present The cardiac output is also increased about 50 per cent above normal in the latter stage of pregnancy It has been claimed that the placenta acts like an arteriovenous leak and that the circulatory adjustments in pregnancy may therefore be compared to those of patients with an arteriovenous fistula This is not proved The velocity of blood flow is increased The basal metabolic rate may rise up to 25 per cent (increased oxygen consumption of the fetus) Often the blood pressure rises slightly (Jensen) but more frequently it remains normal There is a marked retention of sodium probably due to a hypersecretion of aldosterone A peculiar disease of the myocardium which appears in the puerperium was described in the chapter on myocardial diseases (Sodeman)

The added demands of the placenta the greater weight of the patient the increased basal metabolic rate difficulties in respiration and certainly many other factors for the most part unknown at present increase the minute volume and the load on the heart The heart is anatomically larger during pregnancy (Tandler) The adverse effect of many aggravating factors gradually diminishes toward the end of pregnancy when lightening appears No available explanation is satisfactory for this phenomenon The circulatory disturbances mentioned begin to appear at about the twelfth week of pregnancy

Contraindications Frequently a certain valvular lesion is regarded as a contraindication to pregnancy Thus for many years mitral stenosis in any stage was considered particularly dangerous and few physicians hesitated to interrupt pregnancy in the presence of this lesion No less an observer than Mackenzie pointed out that mitral stenosis constituted a very common source of peril and most physicians of his time accepted the same view According to modern experience patients with mitral stenosis actually seem to offer a greater danger than those with other valvular lesions We are heartily in accord with this opinion Many other observers however regard aortic lesions as contraindications despite the fact that it is precisely in this lesion that full compensation is often maintained for many years

The presence of atrial fibrillation is considered by some authorities to be a bar to pregnancy while others emphasize correctly that it is not an added burden per se

The important question it seems to us is not *which* valvular lesion is present but how marked it is the extent of compensation the degree of functional capacity of the patient and the condition of the myocardium are of importance In this connection the four classes of functional capacity defined by the New York Heart Association according to the condition of the patient

are of great value in providing a better guide for the management of an individual case

Clinical Findings Cardiac examination of patients late in pregnancy reveals displacement of the heart due to the high position of the diaphragm This may lead to an erroneous diagnosis of cardiac dilatation A systolic murmur is audible (50 per cent) over the pulmonary artery and is explained by the kinking of this vessel (Landt and Benjamin) it disappears during deep inspiration The second pulmonic sound is often accentuated when the elevated diaphragm pushes the conus of the right ventricle closer to the chest wall The same mechanism may force the ascending aorta toward the chest wall in other cases and lead to an accentuation of the second aortic sound As a consequence of the cardiac displacement the electrocardiogram shows a deep Q wave in lead III in about 30 per cent of the cases

According to Mackenzie extrasystoles are very common and appear in about 50 per cent of healthy women during pregnancy Attacks of paroxysmal tachycardia in this period also have been repeatedly described These arrhythmias usually disappear shortly after delivery They are indicative of some change in the myocardium but the precise mechanism is unknown

Albuminuria is common and ankle edema due to pressure of the enlarged uterus on the iliac veins is also found often There is a low oncotic pressure A loud physiologic murmur in the presence of these findings may make it difficult to exclude an organic heart disease It is even harder to rule out beginning decompensation in a patient who is known to have an organic heart lesion In the presence of edema the status of the liver is important in excluding right ventricular failure but examination of this organ may be difficult in advanced pregnancy It is easy to diagnose left ventricular failure (pulmonary congestion) by the appearance of basal rales and a prolonged circulation time

Prognosis and Complications The heart disease may be so trifling that one need expect no risk from a pregnancy On the other hand it may be of such a degree that complications will develop with certainty The heart disease may be prohibitive In women over 35 years of age the danger of complications is particularly great

Dissecting aneurysms occur in pregnant women Spontaneous abortions are rare in cardiac patients Irregular menstruation and early menopause are common

The greatest strain on the heart occurs when the pregnancy is 28 weeks old and for 24 hours after delivery

According to older observations one out of every five pregnant women with chronic rheumatic heart disease develops congestive heart failure for the most part in the seventh or eighth month of pregnancy If decompensation appears there is an even chance of going through the term without difficulty There is no doubt that the danger of pregnancy in chronic heart disease was often overemphasized and that modern methods afford a much greater opportunity for cardiac patients to deliver a healthy baby without endangering their lives According to Hamilton the mortality of patients with compensated cardiac

lesions is 2 5 per cent Those which he places in his unfavorable group have a mortality of 16 7 per cent and the mortality in patients with atrial fibrillation is 33 per cent The death rate in patients with pregnancy and heart disease has fallen in recent years from 8—10 per cent to 2—3 per cent (Jensen Gordon) There is however always a great deal of uncertainty which precludes any dogmatism One of us observed a patient with a moderately advanced but compensated mitral stenosis who went through 12 normal deliveries without medical supervision We have also seen other patients with so mild a mitral stenosis that they were unaware of its existence and yet died immediately after delivery from a fulminating pulmonary edema

It is always helpful to know how previous pregnancies were tolerated If decompensation developed in a previous pregnancy in all probability a second pregnancy will lead to serious complications

Pulmonary edema may appear at any stage of pregnancy in mitral stenosis although the valvular lesion seems slight Help may come too late even if expert therapy is prescribed

The development of pulmonary edema during delivery or a few hours post partum is a dramatic and very serious complication particularly in patients with mitral stenosis Acute pulmonary congestion caused by strain during delivery and overfilling of the lesser circuit with blood returning in huge quantities from the pelvic veins are responsible for this dangerous complication We have not encountered it since we advised the obstetrician to administer morphine for the first 12 hours post partum to every woman with heart disease and suggested a phlebotomy in those patients whose delivery is more or less bloodless Prolonged labor shold be avoided by all available means

Another serious complication is the development of subacute bacterial endocarditis following delivery One per cent of cardiac patients in a large series of carefully observed cases developed this complication To avoid this tragic event we advise 600 000 units of procaine penicillin daily for five days following delivery Some authors recommend also the intramuscular injection of streptomycin

It has often been maintained that cardiac patients whose pregnancy goes to term without complication and ends in a normal delivery afterward do not feel as well and their ability to work diminishes Some statistics show however that one or two pregnancies are often tolerated well without detriment to health and without shortening life Frequent pregnancies at intervals of one or two years are however dangerous Here also an evaluation of each patient is necessary in determining the course

Medical Advice In the evaluation of every case the age of the patient the degree of the lesion the status of the myocardium the functional capacity of the heart the reserve power and the history of previous failure must be considered

If a woman with organic cardiac disease asks whether she dare take the risk of pregnancy the answer must be no in the presence of congestive heart

failure even if earlier congestive heart failure was present and is now prevented by continuous medication There are patients in this group who reach term and contrary to all expectations have a normal delivery but they are exceptional The statement that delivery is shortened in decompensated patients owing to edema of the tissues remains unconfirmed

In the presence of a fully compensated valvular lesion the patient must be informed about the increased risk involved in pregnancy but in most instances she is willing to undertake it Continuous observation during the pregnancy is necessary beginning with the sixth lunar month the patient must be examined weekly for evidence of heart failure Activities must be reduced periods of rest must be prolonged the nutrition must be adequate and an ample supply of thiamine chloride and iron should be given Lack of thiamine is a common reason for cardiac symptoms and signs in pregnant women Sodium intake may have to be restricted

Valvulotomy in mitral stenosis has been performed successfully during pregnancy Often the operation is better performed after pregnancy terminates

There is no need for and no help can be expected from the prophylactic administration of digitalis before decompensation occurs At term the safest method of delivery is elected and strain should be avoided Until recently caesarian section under ether anesthesia was considered advantageous The patient was thus spared the work of delivery the danger of subacute bacterial endocarditis was reduced to a minimum the most favorable moment for the termination of pregnancy with the patient in the optimal state could be chosen if necessary the duration of the pregnancy could be shortened and sterilization could easily be included in the operation if this were desirable In patients with coronary sclerosis caesarian section is still preferred Many obstetricians are now against a caesarian section in rheumatic heart disease since the mortality of patients in whom surgery has been performed is a little greater but these cases usually have been more seriously ill It has been shown in a large series of observations that the dangers of delivery at term for the well prepared patient were grossly exaggerated This trend away from caesarian section may change however with new methods of preventing complications (antibiotics and anticoagulants which prevent infection thrombosis and pulmonary embolism)

Pitressin and ergotamine preparations are best avoided

How great the accomplishments of modern management of pregnancy in cardiac patients can be is illustrated by the following two sets of statistics collected in the pre penicillin era

In a series of 1089 patients in whom pregnancy was complicated by *rheumatic* heart disease the total mortality was 1 per cent and the cardiac mortality was only 0 17 per cent (Mendelson) In a series of 43 cases in which there was cardiac involvement but a spontaneous delivery and 18 cases of caesarian section there was no mortality (Frey and Lardi)

If the patient is seen for the first time in the early weeks of pregnancy (the first three lunar months) with signs of decompensation therapeutic abortion is indicated Religious principles must be considered the situation must be explained to the patient and her family and the decision must be made by them It has also been recommended that the patient be sterilized at the same time if decompensation begins in the first five months of pregnancy These operations are of course performed after the cardiac status is improved as far as possible by the usual treatment

If decompensation starts after the fifth month it is advisable to wait for delivery at term and to keep the patient under continuous close observation and treatment Physical and mental rest and sodium free diet are usually required Digitalis and mercurial diuretics are not harmful Lactation is permitted if no congestive failure exists Often a marked improvement occurs in the last weeks of pregnancy when the load on the heart is reduced and the risks are no greater than with an operative procedure In the opinion of many obstetricians section is indicated only when there are definite obstetrical indications for it The first stage of delivery is *shortened and the use of an analgesic or ether low spinal* caudal anesthesia is recommended whereas at full dilation the application of a low forceps shortens the second stage

While the blood pressure in the healthy woman scarcely changes during pregnancy patients with essential hypertension show an increase of pressure There is also evidence of impairment of kidney function Persistent increase of blood pressure to values over 200 mm Hg from the beginning are indications for an interruption of pregnancy For some a diastolic blood pressure over *100 mm Hg is an indication for interruption of an early pregnancy* Infant mortality is high in these cases The danger of toxemia of pregnancy is great with papilledema albuminuria and headache According to Browne and Dodd a blood pressure of 150/100 mm Hg at the beginning of pregnancy gives little likelihood of a successful pregnancy for birth of a viable child the chances are no better than 32 per cent Gain in weight albuminuria edema and increase of blood pressure are early signs of toxemia usually occurring after the twenty fourth week of pregnancy Patients with essential hypertension before pregnancy *are often worse off after pregnancy*

According to others patients with moderate hypertension and *even chronic* nephritis tolerate pregnancy well when azotemia is absent Myocardial infarction is compatible with a normal course of the pregnancy provided it does not occur at the end of the term

Patients with a noncyanotic *congenital heart lesion* seem to tolerate pregnancy relatively well In patients with patent septa or a patent ductus arteriosus as well as pulmonary stenosis pregnancy is as a rule tolerated well In patients with mitral stenosis hemoptysis or pulmonary edema may occur only during pregnancy and disappear completely afterward

Patients with atrial septal defects usually stand pregnancy very well In patients *with aortic coarctation the danger of aortic dissection is great*

A marked bradycardia often appears normally for the first few days following delivery

If paroxysmal tachycardia appears therapy with quinidine and procaine amide is permissible in spite of the pregnancy

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Chapter 28

Cardiac Disease and Surgery

PATIENTS AS A RULE tolerate major surgical procedures strikingly well despite the presence of advanced cardiac alterations This is particularly true if congestive heart failure is absent Anxiety about patients in this group often turns out to be unjustified

Since there are dangers inherent in every operation and the hazards of pulmonary embolism in particular are greater in patients with a disturbed circulatory system operations should be restricted to those absolutely indicated If for example roentgen therapy promises the same success one should not operate A repair of a hernia or the replacement of a prolapsed uterus may be omitted and conservative treatment advocated

While the operative mortality was 1.9 per cent in patients without heart disease who underwent a prostatectomy it was three times as great in cardiac patients (Iversen et al) Others found that in coronary sclerosis the mortality increased four times In such patients it has been recommended that nitroglycerin tablets be inserted sublingually several times during the operation (Morrison)

In 257 patients whose ages varied from 35 to 83 12.4 per cent of whom had survived a previous coronary thrombosis the postoperative mortality from cardiac accidents was 4.3 per cent (11 cases) among the 11 mortalities coronary thrombosis occurred postoperatively in seven (Brumm and Willius) Etsen and Proger found in 517 patients with coronary disease a postoperative mortality from all causes of 2.9 per cent The mortality was only 2 per cent in 4154 patients without clinical evidence of heart disease Two of 11 patients with acute myocardial infarction who needed emergency operations died In such case the mortality seems to be definitely higher

With skillful operation and expert anesthesia cardiac strain is not increased (Marvin) Selection of the wrong anesthetic anoxia or otherwise badly conducted anesthesia poor postoperative management as exemplified by the intravenous administration of excessive amounts of fluid may do great harm

In coronary sclerosis the danger of coronary thrombosis is great and the danger is augmented by fall of blood pressure or shock Shock irrespective of its origin is often responsible for multiple arterial occlusions in elderly patients with coronary sclerosis According to some statistics the mortality in patients with healed myocardial infarction is higher than in other cardiacs (Butler et al) on the other hand experience shows that such patients tolerated thyroidectomy astonishingly well when this operation was frequently performed in cardiac

patients The same situation prevails in patients requiring a prostatectomy The heart is strained by hemorrhage large intravenous infusions hypoxia and tachycardia Deliberate lowering of blood pressure by the anesthetist should be avoided

Patients with valvular lesions tolerate surgery very well Atrial fibrillation is no contraindication especially when it accompanies a valvular lesion and not coronary sclerosis Digitalization is important in these patients

Myocardial lesions undoubtedly increase the danger but fortunately primary myocardial lesions are uncommon

The selection of the correct anesthetic is very important Inhalation anesthesia with ether seems most preferable Ether does not damage the heart muscle and has no appreciable influence on blood pressure It practically never causes arrhythmias It paralyzes the peripheral vagus apparatus and thus diminishes the danger of asystole Oxygen should be admixed in ample amounts It is well however to avoid ether if pulmonary complications are present

Ethylene and nitrous oxide are permissible if care is taken to supply sufficient oxygen Ethyl chloride is however known to provoke ventricular fibrillation Cyclopropane anesthesia otherwise very satisfactory should be used in cardiac patients only with great caution since the heart dilates markedly during its administration (Brace et al) Cyclopropane also causes multiple extrasystoles although they are less dangerous than those encountered in chloroform anesthesia While some investigators have noted extrasystolic arrhythmias and tachycardias in 10 per cent of anesthesias with cyclopropane ventricular fibrillation is rare Opinions about the origin of these arrhythmias vary and no explanation is completely satisfactory

Spinal anesthesia invites the danger of a sudden fall of blood pressure particularly in hypertensive patients The anesthetist must do everything to prevent hypoxia and a fall of blood pressure and must avoid the administration of adrenalin or pituitary extracts

Loss of electrolytes (potassium) is an important reason for postoperative heart failure

Intravenous administration of barbiturates is to be avoided in patients with a damaged or overdilated heart muscle Barbiturates serve in the animal experiment as preferred compounds for inducing myocardial damage

Because of the presence of hypoxia nitrous oxide should be avoided in patients with coronary disease

Consideration should be given to the fact that excessively rapid absorption of local anesthetics may be dangerous for the heart The admixture of epinephrine to prevent rapid absorption should be avoided in patients with organic heart disease It may be replaced by preparations of the pituitary

The question of cardiac preparation preliminary to operation has been widely discussed Water retention should be abolished as much as possible and anemia corrected Positive evidence of the advantage of a prophylactic digitalization is not available and preparation of the patient by this method has been abandoned If a patient requires an emergency operation and shows evidence of

decompensation or a very fast ventricular rate with atrial fibrillation much can be accomplished with an injection of strophanthin or one of the pure glycosides (digoxin cedilanid) while preparations for the operation are completed Emergency operations must be performed regardless of the cardiac status of the patient

Cardiac arrest (via reflexes) is an operative complication which is reported more frequently at present Immediate opening of the chest (fourth intercostal space) and cardiac massage are necessary within three minutes (p 581) External electrical stimulation of the heart may suffice

At present, surgeons are generally inclined to favor early postoperative ambulation We agree with this measure but believe it should be done with care since newly formed thrombi are easily dislodged Blodgett and Beattie found the incidence of deep vein thrombosis even somewhat higher in patients who were made active at an early stage

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Chapter 29

Disturbances of Cardiac Rhythm

Clinical Aspects of Extrasystoles

The disturbance of cardiac rhythm caused by extrasystoles (premature beats) has been known ever since the human pulse was felt Until the end of the last century however the chief cause of the intermittent pulse was unrecognized despite the fact that after the work of Marey extrasystoles were induced very often experimentally to aid in the study of fundamental questions of cardiac physiology After the similarity between premature contractions caused in animals by mechanical or electrical stimuli and those appearing in man was recognized by Wenckebach and Cushny this disturbance was found to be the most common cause of cardiac irregularity

Definition Extrasystoles are premature contractions interrupting cardiac rhythm caused by the preceding beat they are coupled to this beat by an interval which is usually short and constant for a given case By this definition premature beats caused by other mechanisms (parasystole or interference dissociation) are excluded

Origin and Appearance While they may originate in any part of the heart two main groups are distinguished atrial and ventricular extrasystoles In rare cases extrasystoles originate in the sinus or in the atrioventricular node For practical clinical purposes it is immaterial from what part of the atrium or ventricle the extrasystole emerges

Extrasystoles may appear singly with a long chain of normal beats between them or they may occur frequently after every few beats or even after every sinus beat In the last case we speak of bigeminal rhythm if two extrasystoles follow each normal beat regularly a trigeminal rhythm exists Many authors incorrectly call the appearance of one extrasystole after two normal beats a trigeminus

All variations and combinations occur If several extrasystoles follow each other we speak of groups of extrasystoles if the chain is longer we may call it a short paroxysmal tachycardia

Electrocardiogram Figure 92 shows three premature atrial contractions which interrupt a regular sinus rhythm They are represented in the electrocardiogram by premature and slightly different looking P waves the atrial extrasystoles are conducted normally to the ventricle

A ventricular bigeminal rhythm is present in figure 93 This tracing was obtained from a 50 year old man who had no evidence of cardiac disease Each normal beat is followed by a ventricular extrasystole

In figure 94 series of ventricular extrasystoles are visible These extrasystoles appeared in a case of rheumatic fever The atrioventricular conduction time in this case is prolonged to 0 26 second



FIG 92 Three atrial extrasystoles

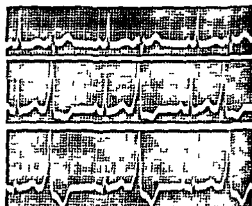


FIG 93 Ventricular extrasystoles in the form of a bigeminal rhythm

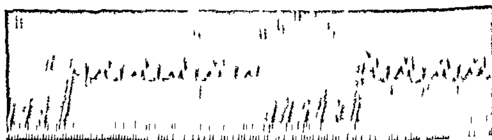


FIG 94 Prolonged atrioventricular conduction time and a series of ventricular extrasystoles

Cardiodynamics Every extrasystole causes a considerable disturbance in cardiodynamics An extrasystole may occur so early in diastole that ventricular filling is negligible The more prematurely an extrasystole appears the smaller is the stroke volume of the extrasystolic contraction and the smaller will be the pulse caused by it If extrasystoles are very premature no pulse is palpable in the peripheral arteries and the contraction is abortive Such an extrasystole advances

little or no blood into the arterial system at the same time during the extra systolic contraction the inflow of blood from the atria into the ventricle is impeded and venous stasis develops Since the postextrasystolic pause is as a rule much longer than the normal cardiac pause of the individual the stroke volume of the first normal beat following the extrasystole is correspondingly larger and the associated pulse stronger Whereas an extrasystole propels too little blood into the arterial system the situation is balanced by the first normal beat after the



Fig 95 Pulse changes typical of extrasystoles (see text)

extrasystole and circulatory disturbance is prevented The minute volume remains normal even if some of the systoles (extrasystoles) eject little blood into the arteries Thus a patient may have many extrasystoles per minute for a lifetime and still not suffer from any disturbance of the circulation

In figure 95 the pulse tracing and the electrocardiogram of a patient with atrial extrasystoles are reproduced An atrial extrasystole appears after the second normal beat The extrasystole causes a premature smaller pulse wave Due to the postextrasystolic pause the first postextrasystolic pulse wave is much larger An alternating pulse is visible for the first few postextrasystolic beats

Symptoms Most extrasystoles provoke no sensation Patients are frequently encountered in whom multiple extrasystoles or bigeminal rhythm have persisted for months or years without attracting attention or causing any symptoms In other instances the attention of the patient is directed to the disturbance accidentally by the awareness of an irregular cardiac rhythm in the stillness of the night when one ear rests upon the pillow through the palpation of the pulse or through the remark of a physician Under these circumstances the patient notices the irregularity but otherwise he does not feel it

At times extrasystoles create considerable annoyance The symptoms vary Rarely the extracontraction itself is felt as an unpleasant impact Patients often give very vivid descriptions of their sensations so that the diagnosis can be made on the basis of the history Some report a sensation like a sudden blow others a brief awareness of some event in the cardiac area which is described differently according to imagination and education It is a sudden jumping kicking or a sudden blow or somersault Sometimes it is referred to as a skipping of the



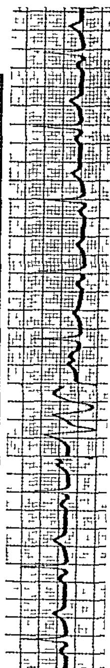


FIG 96

FIG 97 →

FIG 96 Multiform ventricular extrasystoles

FIG 97 Series of multiform extrasystoles in a patient with coronary sclerosis death occurred suddenly one day after this tracing had been taken This type of extrasystoles not rarely precedes ventricular fibrillation

heart other times a sudden sharp painful sensation is felt In neurotic patients who observe the heart and the sensations in the cardiac area carefully a pain may be felt with every extrasystole which makes the whole body twist as if the patient had touched a live wire Slight faintness may also appear Frequently the pauses after the extrasystole are perceived unpleasantly the patient has the sensation that his heart suddenly stood still He anxiously waits to see 'whether it will begin to beat again' This sensation is interesting in view of the shortness of the postextrasystolic pause Most often however the normal beat after the extrasystole is felt as a strong contraction and produces the sensation described above This is natural since the first normal beat after the extrasystole expels a very large stroke volume In aortic regurgitation with a large left ventricle and a larger stroke volume even with regular cardiac action the postextrasystolic beat is particularly unpleasant

Of interest is the dry short cough caused by an autonomic reflex occuring in some persons with every extrasystole

Signs If the existing rhythm is interrupted by premature beats which are followed by a long pause the correct diagnosis can be made in most cases without an electrocardiogram The earlier the extrasystole occurs and the more incomplete the filling of the ventricles the louder is the first heart sound particularly over the apex Owing to the small stroke volume the second heart sound is soft When extrasystoles occur very early the second heart sound may be absent since the semilunar valves are not opened by the abortive systole

Not rarely extrasystoles disappear at the time of the examination They may vanish with any measure which increases the heart rate and consequently shortens the length of diastole Therefore exertion and excitement

usually abolish extrasystoles Often they appear however a short time after exertion when the initial tachycardia subsides Sometimes they are elicited by carotid pressure or after inhalation of amyl nitrite (Scherf)

Differential Diagnosis In a majority of cases the occurrence of a premature contraction disturbing the existing rhythm with a succeeding long pause permits the diagnosis without graphic registration Under certain conditions however difficulties arise

If extrasystoles are multiple and occur irregularly they may be confused with atrial fibrillation The differentiation will be discussed later

In patients with a continuous bigeminal rhythm in which the first sound of the extra contraction alone is heard gallop rhythm is occasionally diagnosed because a third heart sound is heard shortly after the two normal sounds Since extrasystoles usually disappear on acceleration of the heart any slight exertion — sitting up and lying down a few times — will abolish the extrasystoles this exercise will usually accentuate the gallop rhythm

Occurrence Extrasystoles may appear at any age Repeatedly they have been detected during auscultation of the fetal heart sounds (Antoine) Most physicians believe that there is rarely a healthy individual who has never exhibited an extrasystole They come and go without detectable reason and are in most cases devoid of any importance

In other instances definite reasons for their occurrence can be found In one individual they appear with meteorism or constipation in another with deep breathing In one patient they are found only on deep inspiration in another only with deep expiration They may occur only before menstruation and are a common event during pregnancy For the most part they are present only at rest but in rare instances they appear during or immediately after exertion

Certain drugs and certain substances like caffeine and nicotine may cause them The extrasystoles due to drinking strong coffee and after smoking have been known for many years and were discussed even at the time when one spoke only of an intermittent pulse Chloroform and cyclopropane anesthesia often elicit extrasystoles Premature contractions are also not rare following an injection of adrenalin and allied substances One of the more important types of clinical extrasystoles is the variety that appears during treatment with digitalis

Extrasystoles are occasionally caused by reflexes That premature contractions may be elicited by carotid pressure or on deep breathing was mentioned above The literature on extrasystoles caused by mechanical or chemical irritation of the respiratory tract or from the digestive tract is large Extrasystoles appear on distention of the stomach (Pribram and Mayer) on the insertion of a tracheal tube during cyclopropane anesthesia (Reid and Brace) in patients with gall bladder disease and in those with a hiatus hernia (Kaestner) Certain hypothalamic centers have been shown to be an important link in these reflexes (Allen Brown et al)

If extrasystoles appear during diphtheria coronary disease pneumonia or scarlet fever they often indicate a lesion of the myocardium and have diagnostic

importance Extrasystoles due to an organic heart disease often but not invariably are recognized electrocardiographically by the fact that they seem to arise from multiple foci

Extrasystoles have been described in allergic reactions (Harkavy)

Extrasystoles may persist for many years in the same individual Walsh observed them on himself for 40 years

Mechanism The finer mechanism of origin of extrasystoles is still unknown in spite of the ease with which they can be elicited by mechanical electrical or chemical stimuli

Extrasystoles are caused by different disturbances In rare cases a circus movement or re entry mechanism is active In a majority of cases however firing of an impulse in an abnormal focus initiated by the beat preceding the extra systole takes place (Scherf and Schott)

Clinical Importance While extrasystoles arise from an abnormal type of stimulus formation it is incorrect to assume the presence of cardiac disease simply because extrasystoles exist There are many arguments to support the assumption that the abnormal stimulus formation takes place in one fiber a center It is easy to conceive that the structure of the cell in one of the innumerable muscle fibers becomes altered leading to an abnormal depolarization of this cell and to a premature contraction Indeed one may assume that frequently in other organs of the body a single cell may be abnormal in a similar way without the organ to which it belongs being diseased But such an abnormality is rarely recognizable in other organs In the heart however if a stimulus formed by an abnormal center is above threshold it may excite first the neighboring cells and then the entire heart thereby being easily detected

If extrasystoles occur the only deduction permissible at first is the presence of a disturbance in a restricted area This disturbance is probably limited to a single cell If the remainder of the heart shows nothing abnormal — no anginal pain or infectious disease i e no condition in which cardiac damage is suspected — then the extrasystoles are usually devoid of any significance In the appraisal of the case it is immaterial whether few or many extrasystoles are present

Since extrasystoles may constitute even an early sign of a pathologic process in the myocardium every patient in whom premature contractions are found deserves a careful examination If no abnormalities are discovered he should be observed over a period of time In some cases only prolonged observation permits one to decide whether a purely local and negligible alteration exists or whether the extrasystoles indicate the development of a cardiac disease which otherwise would have escaped detection

If the physician is consulted by a patient who reports that extrasystoles have been present for years the negative result of even a single thorough examination will be sufficient to show that a harmless disturbance exists in a person with a healthy heart

Most extrasystoles have no prognostic significance for prognosis depends upon the cardiac status

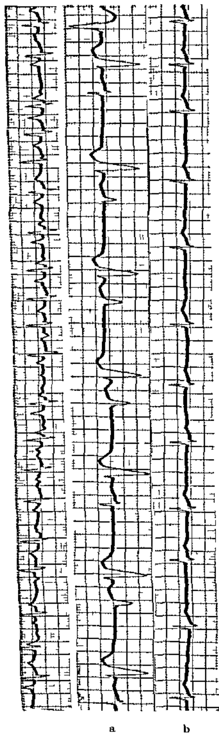


FIG 98 FIG 99

Multifocal ventricular extrasystoles always indicate myocardial damage and are therefore a finding of importance (figures 96 and 97)

Figure 96 shows an instance of multiform extrasystoles in lead II This tracing was taken from a 61 year old man with coronary sclerosis and angina pectoris The atrioventricular conduction time is prolonged to 0 26 second The width of the QRS complex is 0 12 second and the T waves are inverted Each sinus beat is followed by a ventricular extrasystole but their form continually varies The extrasystoles seen in healthy people always have the same form even if they persist for years

In an overwhelming number of cases unifocal extrasystoles are harmless but they may also accompany myocardial disease In conditions in which atrial fibrillation is common such as mitral stenosis hyperthyroidism and coronary sclerosis atrial extrasystoles may precede the onset of fibrillation for some time

A typical disturbance appearing in any age but found especially often in elderly patients is the arrhythmia shown in figure 98 Atrial extrasystoles originating in many foci and shifting of the pacemaker with varying forms of T waves are seen This arrhythmia often precedes atrial fibrillation

Treatment If an individual does not feel the extrasystoles and if examination as well as observation reveals a healthy heart it is a serious mistake to draw the attention of the

FIG 98 Shifting pacemaker and multiform atrial extrasystoles

FIG 99 Multiform ventricular extrasystoles partly bound to ectopic idioventricular beats in a 67 year old patient under treatment with digitalis (a) Following the administration of 5 grams of potassium chloride the extrasystoles disappeared (b)

patient to the cardiac irregularity or to treat it The layman is readily inclined to consider any irregularity of the ever constant rhythm of the heart as a serious disease

If a healthy individual consults the physician because he feels the extrasystoles and the examination reveals no cardiac disease the harmlessness of the disturbance should be explained to the patient and an endeavor made to convince him that he may lead a completely normal life It is well to point out that this disturbance occurs chiefly at rest while physical exertion which precipitates symptoms in organic heart disease causes no discomfort and as a matter of fact usually abolishes the extrasystoles

If the physician omits explanations or if he lacks the necessary knowledge and authority for this purpose indeed if he speaks of a mild heart muscle irritation and suggests restriction in some activities the patient simply sees his own conception of an organic heart ailment thoroughly confirmed He observes himself more carefully and with greater anxiety counts the number of premature contractions per minute observing all the details of the sensations caused by them The anxiety neurosis which soon develops from a harmless phenomenon can be treated only with difficulty and patience If the physician succeeds in convincing the patient that the extrasystoles are meaningless they are usually soon disregarded This is accomplished more readily if the physician insists authoritatively that the patient is a healthy person and should lead the life of a normal individual Nothing will convince the patient so readily of the innocence of his disturbance as lack of prohibitions and restrictions Furthermore the patient should be instructed not to watch the rate or rhythm of his pulse

The result of this therapy depends upon whether or not the patient can be convinced that the extrasystoles are meaningless and that they can be dismissed as unimportant

If they occur in organic heart disease the extrasystoles per se rarely require drug therapy Exceptions are extrasystoles in coronary thrombosis which may be precursors of ventricular fibrillation and the previously mentioned extrasystoles in diseases that are often accompanied by atrial fibrillation

If definite factors are found to release extrasystoles an attempt should be made to eliminate them Often the correction of marked meteorism a high diaphragm a severe constipation and gall bladder disease or cessation of smoking will permanently abolish the extrasystoles

Treatment with drugs is not necessary in most cases Such therapy affords relief only for the duration of administration As soon as the patient discontinues treatment the extrasystoles recur and the patient becomes more upset than before

In addition to the conditions mentioned earlier the administration of drugs is indicated when the extrasystoles multiply in a threatening manner or evoke so many unpleasant complaints that it seems advisable to remove them at least temporarily in order to convince the patient that palliative treatment and control of his condition is possible It is however advisable to inform the patient before instituting treatment that extrasystoles will probably recur when the administration of the remedy is stopped

Since Wenckebach s recommendation quinine and its much stronger isomer quinidine (Frey) are regarded as the most effective remedies for abolishing extrasystoles because they diminish the irritability of the heart and depress stimulus formation and conductivity If suitable doses of these drugs are administered extrasystoles are abolished in most instances

Since quinidine is rapidly eliminated from the body it is advisable to give small doses frequently As with all forms of cardiac therapy the opportunity to watch the success of the treatment permits adjustment of the therapy to the needs of the patients A capsule or tablet containing 0 2 Gm of quinidine sulfate is prescribed and the patient is advised to take it four or five times a day The first dose should be given as early as possible in the morning the last is given late in the evening If these doses do not suffice the single doses are increased until *the extrasystoles disappear*

A second remedy that removes extrasystoles regularly is digitalis It may seem strange that a drug which frequently produces extrasystoles should also be employed to abolish them It happens however that extrasystoles appear during digitalis therapy only under specific conditions (see digitalis therapy) As a matter of fact practically every substance which causes extrasystoles in certain doses may abolish them in others This is true for example with potassium magnesium procaine and even quinidine The extrasystoles which are not the consequence of digitalis disappear during digitalis treatment Often small doses such as 0 2 Gm daily for four or five days suffice for this purpose One disadvantage of this procedure is that many patients knowing that digitalis is given for heart disease become frightened when this remedy is mentioned It is however rarely necessary to prescribe digitalis to abolish extrasystoles A rare indication is multiple extrasystoles requiring drug treatment and at the same time the presence of idiosyncrasy of the patient to quinidine

In recent years procaine amide (Pronestyl) has been introduced into the therapy of cardiac arrhythmias It can be given orally and is not rapidly destroyed by enzymes as is procaine The dose is 0 50—0 75 Gm three or four times daily Quinidine should remain the drug of choice Pronestyl more useful in ventricular than atrial extrasystoles is given when hypersensitivity prevents administration of quinidine The doses of Pronestyl required for the treatment of extrasystoles and paroxysmal tachycardia are three times as large as those of quinidine (Schaffer) The side effects of both compounds are similar

Often it is possible to abolish extrasystoles particularly those due to digitalis with potassium salts given orally (figure 99) This treatment has considerable interest and will be discussed in the chapter on paroxysmal tachycardia

CLINICAL ASPECTS OF ATRIAL FIBRILLATION AND ATRIAL FLUTTER

Atrial Fibrillation

Atrial fibrillation was known for a long time to those who performed animal experiments Formerly the condition was called arrhythmia perpetua before it

was realized that the irregularity may disappear spontaneously or be abolished by treatment Total disorder of the cardiac rhythm in clinical atrial fibrillation was recognized as delirium cordis by physicians of the last century The identity of both was suggested by Cushny and Edmunds but it was not proved until the introduction of electrocardiographs in institutions (Rothberger and Winterberg as well as Lewis)

Incidence Atrial fibrillation is present in approximately 50 per cent of patients who seek hospitalization because of cardiac diseases It is very common in rheumatic mitral lesions in hyperthyroidism and in coronary sclerosis But fibrillation may also occur in other valvular diseases as well as in myocardial lesions and hypertension It is not an unusual complication of diseases frequently accompanied by myocarditis such as pneumonia and typhoid fever but it is rather rare in patients with syphilitic aortitis and syphilitic aortic regurgitation Although uncommon in cor pulmonale and bacterial endocarditis every cardiologist has observed it in these conditions

Atrial fibrillation has been observed in an infant three months old (Coldbloom and Segall) It is occasionally seen in otherwise apparently healthy persons after violent exercise

Occasionally atrial fibrillation is discovered in a patient whose heart has been completely normal through decades of careful observation In some of these patients some latent cardiac pathology myocarditis accompanying streptococcic infection for instance might have existed and have escaped detection while the fibrillation persisted

Electrocardiogram Figure 100 shows a typical instance of atrial fibrillation in the 3 standard leads The tracing was obtained from a 61 year old man with coronary sclerosis The irregularity of the ventricular activity is clearly visible Characteristic however are the irregularly formed fibrillation waves (F waves) which replace the normal P waves

Dynamics Patients with atrial fibrillation in whom less than 80 atrial stimuli per minute reach the ventricles due to a high vagal tonus or slow conductivity of the specific tissue feel normal If the heart of these patients is otherwise normal the fibrillation is asymptomatic and is discovered only by chance Occasionally one even sees patients with organic heart disease — for instance a slight rheumatic mitral stenosis — *who alternate between fibrillation and sinus rhythm without* being aware of the difference

Unfortunately these cases represent the exception As a rule the conduction system transmits more than 80 stimuli per minute to the ventricles and with faster rates symptoms increase The inadequate output and the fall of the minute volume associated with it lead to a feeling of weakness and faintness Dyspnea on exertion may appear but often is not prominent since the rapid activity of both right and left ventricles leads to venous and hepatic congestion i e to signs of right heart failure and not to pulmonary congestion In fact the appearance of right ventricular failure often coincides with the disappearance of any existing pulmonary congestion

The engorgement of the neck veins causes a sensation of fullness and constriction The enlargement of the liver leads to nausea as an early symptom and later to vomiting and right hypochondrial pain

The tachycardia may cause anginal pain especially if the patient has coronary sclerosis It may also cause fainting and other cerebral phenomena particularly in patients with cerebral vascular sclerosis Too rapid ventricular action in patients with atrial fibrillation may lead to Stokes Adams attacks and even to sudden death although the latter event is not unequivocally proved



FIG 100 Atrial fibrillation and the effect of digitalis on the RS T segments and T waves

Signs The complete disorder of the heart rhythm usually permits the diagnosis without difficulty If the ventricular rate is slow the arrhythmia is not so easily recognized but it becomes more apparent with prolonged auscultation A slight increase of the heart rate by moderate exertion brings out the arrhythmia more distinctly

With the appearance of atrial fibrillation and increase of the ventricular rate the blood pressure falls if venous pulsations are visible in the veins of the neck atrial waves are absent

Due to the prolonged tachycardia signs of congestive heart failure may appear even if the heart is otherwise healthy The high ventricular rate impairs cardiac blood supply and therefore leads to dilatation Relative mitral and tricuspid regurgitation may appear in an otherwise healthy heart if the fast ventricular rate in atrial fibrillation remains uncontrolled for a long time

Differential Diagnosis In most cases it is easy to make the diagnosis without resort to graphic methods The differentiation between multiple irregularly appearing extrasystoles and atrial fibrillation may be difficult In these cases

an exercise test or the inhalation of amyl nitrite permits differentiation since extrasystoles usually vanish if tachycardia shortens diastole and the heart rhythm temporarily becomes regular Under the same conditions the arrhythmia due to fibrillation becomes more obvious since now more stimuli are conducted to the ventricles With an arrhythmic heart action and a rate exceeding 120 atrial fibrillation is usually present

Sometimes respiratory arrhythmia is confused with atrial fibrillation particularly if the relation between the respiratory phases and the arrhythmia is somewhat atypical The disappearance of the arrhythmia when the patient holds his breath leads to the correct diagnosis

One often hears the remark that the patient fibrillated less today than on previous examinations This statement is incorrect The fibrillation in such cases remains unchanged but the ventricular rate is slower and the arrhythmia is less distinct

Mechanism Attempts to explain the abnormal mechanism causing atrial fibrillation on the basis of pathologic structural changes have been abandoned While it is true that the condition is common in some cardiac diseases and rare in others and abnormal histologic findings have been repeatedly described there is general agreement that atrial fibrillation is often an abnormal functional disturbance without anatomic alterations

For many years the opinion prevailed that atrial flutter and fibrillation are caused by a rapid circus movement of a central or mother wave in a closed path *It is impossible to discuss in this connection the fascinating and ingenious* work that has been performed in order to explain this common disturbance The reader is advised to consult textbooks of electrocardiography or monographs on the subject to obtain such information

Recent investigations have shown that these arrhythmias can be explained better by a rapid stimulus formation in a center (Scherf et al) (figure 101) In atrial flutter one center forms the impulses while in fibrillation one or more centers are active (Scherf et al) There are still authors who maintain that atrial flutter and fibrillation are caused by a circus movement mechanism In flutter they would have to explain why it persists when the path around the venae cavae is interrupted by a broad ligature across the sinus node and the neighboring tissue (Scherf) In flutter and in fibrillation they would have to explain why cooling of the tip of the left atrial appendix on which aconitine had been applied in order to elicit them immediately stops these disturbances of rhythm and why they reappear when cooling is discontinued (Scherf et al)

Atrial (and ventricular) fibrillation may appear in a somewhat damaged heart the metabolic state of which is abnormal if one single stimulus falls in a certain period the so called critical or vulnerable period early in diastole At this time an *electrical or a light mechanical stimulus* — *simple touching* of the heart for example — or a natural stimulus in the form of a premature extrasystole initiates fibrillation It was pointed out before that in patients with mitral stenosis or hyperthyroidism atrial extrasystoles often precede atrial fibrillation It may

be assumed that one of the extra systoles occurred precisely during the vulnerable phase and set up the fibrillation During this vulnerable phase a few hundredths of a second at the end of systole and at the onset of diastole one stimulus may lead to rapid firing of impulses

Important for the understanding of atrial fibrillation in mitral stenosis is the experience that under certain conditions stretch exerted on the right atrium may elicit this arrhythmia (figure 102)

Duration Attacks of atrial fibrillation last for variable periods Often a paroxysm persists only for a few hours while we have seen attacks last no longer than a few seconds In other cases the disturbance remains for months or years If attacks of atrial fibrillation recur frequently their management and clinical importance also depend upon the ventricular rate With higher rates they have the same importance as attacks of paroxysmal tachycardia

Treatment In slow fibrillation that is atrial fibrillation with a slow ventricular rate no special treatment is required To be sure such patients tolerate effort somewhat less than people with normal cardiac action because the increase of heart rate on exertion is usually greater Patients with atrial fibrillation are however often encountered who for many years show no other symptoms or signs



Fig 101 Dog experiment Atrial fibrillation was created by the application of crystalline aconitine on the appendix of the right atrium Cooling the area of application stopped the fibrillation and restored sinus rhythm (center of tracing) interruption of the cooling permitted the atrial fibrillation to reappear This result cannot be explained by the circus movement theory it speaks in favor of rapid firing off of impulses in a center



Fig 102 Atrial fibrillation had been induced in a dog in the same manner as described in figure 101 It disappeared after 56 minute Stretching the wall of the right atrial appendix leads to temporary reappearance of the fibrillation

The abnormal impulse formation in the atria during atrial fibrillation is of less importance than the ventricular rate — fibrillation is proportionately more harmful as the ventricular rate rises Therefore treatment is aimed chiefly at reducing the ventricular rate and keeping it low With some exceptions (febrile disease rheumatic fever pulmonary embolism hyperthyroidism) this is possible with the aid of digitalis By increasing vagal tonus and thus inhibiting the atrioventricular conduction as well as by a direct action on the muscle fibers diminishing their conductivity digitalis reduces the ventricular rate The fibrillation in the atria proceeds uninfluenced Rarely does it stop during the administration of digitalis The treatment is easy to carry out and the results are good Only in the above named conditions is a slow ventricular rate obtained with difficulty

Since part of the action of digitalis is symptomatic in reducing the ventricular rate the question is often asked whether it would not be wiser to abolish the fibrillation itself by means of quinidine As a matter of fact one can succeed in restoring sinus rhythm in 70 to 80 per cent of the cases by administration of quinidine sulfate Nevertheless the treatment is rarely used

At first some important contraindications must be considered With long lasting fibrillation mural thrombi may form in the atrial appendices and when powerful atrial contractions are again instituted upon the return of normal rhythm these thrombi may be released and produce fatal embolism Unfortunately such accidents are not rare and are regrettable since the administration of quinidine to patients with atrial fibrillation who respond well to digitalis is not obligatory but only an elective method of therapy It has also been pointed out that marked dilatation of the left atrium as it occurs in mitral stenosis represents a contraindication to quinidine treatment because thrombi seem to form more rapidly in overdistended atria Finally any evidence of cardiac failure or myocardial damage contraindicates the administration of quinidine since large doses of the drug are often necessary and quinidine is a cardiac depressant When quinidine is used according to many statistics 2 to 4 per cent of the patients die suddenly from the above mentioned embolisms ventricular fibrillation and cardiac or respiratory standstill If anticoagulants are given for 14 days prior to administration of quinidine the formation of new atrial thrombi is prevented and the danger of systemic embolism is diminished

Moreover experience shows that the normal rhythm often does not persist after quinidine succeeds in restoring it Sooner or later the fibrillation reappears particularly in the three conditions with which it is most frequently associated rheumatic mitral stenosis hyperthyroidism and coronary sclerosis Thus the patient is exposed to the danger by quinidine therapy and shortly after treatment ends he fibrillates again Furthermore such patients feel just as well after successful slowing of the ventricular rate with digitalis as they would if sinus rhythm were present they fail to note any improvement when the atrial fibrillation is removed and often do not enjoy any benefit In some cases of mitral stenosis the restoration of atrial activity will improve compensation In many

other cases the dilated atria do not contract even when sinus rhythm is present these patients derive no benefit from quinidine therapy In mitral stenosis a long diastole is necessary in order to permit adequate filling of the left ventricle Marked slowing of the heart is often impossible with digitalis as long as sinus rhythm exists but is easily accomplished when atrial fibrillation appears There fore patients with mitral stenosis often feel better when fibrillation replaces sinus rhythm The same holds for patients with attacks of paroxysmal atrial fibrillation which can be controlled by digitalis It is also of interest that subacute bacterial endocarditis occurs only rarely with atrial fibrillation It is therefore clear that one should seriously consider whether or not defibrillation with quinidine would be of advantage for a given patient

It is an old clinical rule not easily explained that pulmonary edema in mitral stenosis and angina on effort in coronary stenosis are rarely encountered after the onset of atrial fibrillation

Thus it happens that even in an active service of a large hospital quinidine is rarely used The presence of indications rather than the absence of contra indications should be the determining factor Quinidine should be given when subtotal thyroidectomy has been performed for hyperthyroidism and when all the symptoms of this condition have vanished with the exception of atrial fibrillation Or it should be used in patients who develop fibrillation during a pneumonia or an infectious disease when the fibrillation persists even though they are otherwise healthy Under these circumstances there is reason to hope that the patient will become entirely well after the fibrillation is abolished and the treatment may be justified

In recent years an attempt has been made to revive quinidine therapy of atrial fibrillation as a routine measure The arguments for this procedure are not convincing and we see no reason to change our attitude

In cases in which defibrillation is to be attempted before quinidine treatment is started the patient should be digitalized until the ventricular rate falls to about 80 per minute As soon as this is accomplished a trial dose of 0 2 Gm of quinidine is given orally to test for sensitivity This must be done because abnormal reactions to quinidine in the form of skin rashes diarrhea and respiratory disturbances are common and unpleasant phenomena Death due to hyper ensitivity has been observed after this one dose (Lone) Kalmansohn and Sampson observed transient ventricular fibrillation following doses of 0 2 Gm of quinidine in two patients In rare cases atrial fibrillation disappears even with this first dose If no untoward symptoms are present on the next day treatment is instituted according to the following plan

Day	*Gm Quinidine Sulfate*
1	3 × 0 20
2	4 × 0 20
3	5 × 0 20
4	6 × 0 20 (or 3 × 0 4 Gm)
5	7 × 0 20
6	8 × 0 20
7	9 × 0 20

Naturally the larger doses are prescribed only if the smaller ones are tolerated Smaller doses (0 2 Gm) are given from 8 a m to 8 p m The larger doses (0 4 Gm) are distributed equally within 24 hours If quinidine causes untoward effects treatment is discontinued In many cases the administration of the smaller doses (0 2 Gm) does not bring the desired result while larger doses such as single doses of 0 6 Gm abolish the fibrillation

On the basis of the estimation of the blood level of quinidine during oral therapy it has been proposed that the drug be administered every 2 hours The results are the same however whether quinidine is given every two hours or three times a day One succeeds in reestablishing sinus rhythm in about 80 per cent of the cases Bedard reversed 89 per cent of his patients with atrial fibrillation to sinus rhythm Four and one half per cent of his patients died suddenly However the doses advised by him were much higher than the average (up to 6 grams of quinidine daily)

If the fibrillation disappears 0 2 Gm is given three times a day for a few more days and then is stopped If fibrillation persists on the eighth day treatment is also discontinued Longer administration of large doses increases the risk beyond reasonable prospect of success If the drug is tolerated well in heavier patients even a dose of 0 5 Gm may be given four times daily on the fifth to seventh day of the treatment The patient must be under close observation and must be confined to bed Due to the atropine like effect of quinidine on the peripheral vagus the ventricular rate may slightly increase when the administration of quinidine is started This is why it is well to avoid the combination of digitalis and quinidine as a routine treatment of atrial fibrillation since quinidine counteracts the effect of digitalis to a certain degree

Thiouracil or radioactive iodine may help in patients with frequent attacks of paroxysmal fibrillation and overfunction of the thyroid

Atrial Flutter

Atrial flutter in man was described in 1910 (Jolly and Ritchie)

Mechanism and Electrocardiogram In this condition the atria contract approximately 300 times per minute that is at a rate in which coordinated movements are still possible Occasionally all stimuli reach the ventricle but usually only a fraction of them (every second third or fourth) is conducted If every fourth beat is conducted regularly to the ventricle the ventricular rate appears normal Very often the number of conducted stimuli varies continually so that diverse arrhythmias appear extrasystoles or atrial fibrillation may be mistakenly diagnosed because of the disturbance of rhythm Atrial flutter a much rarer event than atrial fibrillation appears in the same conditions as the latter and is usually permanent Rarely it appears as a short or longer paroxysm

Figure 103 shows an electrocardiogram of a patient with atrial flutter The patient was a 68 year old man with coronary sclerosis The flutter waves are clearly visible in leads II and III Every fourth atrial wave is conducted to the ventricle (4 1 block) in lead I a 3 1 block occurs once

Diagnosis The clinical diagnosis is possible without recourse to electro cardiography once the existence of this disturbance is suspected and the patient carefully examined

In a minority of cases the rapid regular undulations of the flutter waves are visible if the neck veins are inspected (figure 104)

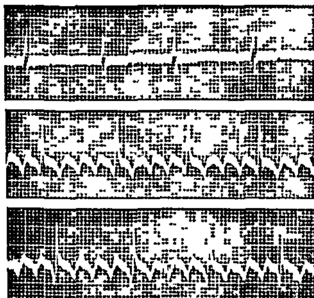


FIG 103 Atrial flutter with 4 1 block

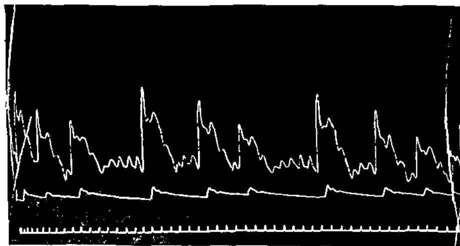


FIG 104 Venous pulse of a patient with atrial flutter and varying A V block the flutter waves (F waves) are clearly visible in the phlebogram

The diagnosis should be suspected in every tachycardia with a ventricular rate of over 100 Ventricular rates of over 300 beats per minute are observed in atrial flutter and full A V conduction While a paroxysmal tachycardia occasionally has this rate it is a usual feature of atrial flutter with full rhythm Frequently with the onset of atrial flutter only every second or third atrial stimulus reaches the ventricle (flutter with 2 1 or 3 1 block) so that the ventricular rate is between 100 and 160 To eliminate a simple acceleration of the heart rate (sinus tachycardia) the patient should be requested to stand to walk a little or if possible to undertake light exercise in the form of climbing stairs or bending In a simple sinus tachycardia a change of posture or slight effort moderately accelerates the rate but this acceleration gradually disappears within a few minutes This is a typical response of the sinus node with normal rate as well as with a sinus tachycardia In atrial flutter however the heart rate remains fixed in all positions even after slight exercise because the abnormal mechanism in the atrium is not influenced by these measures If more strenuous exercise is performed the increased sympathetic tonus improves conduction from atria to ventricles thus a 2 1 block replaces 3 1 block or full conduction appears instead of a 2 1 block The heart rate is increased by exactly 50 or 100 per cent and after a while suddenly returns to its former level The diagnosis is easily confirmed with the aid of the electrocardiogram

Therapy The treatment is not as simple as it is for cases of atrial fibrillation In the latter the rapid and therefore weak atrial stimuli are easily prevented from reaching the ventricle by digitalis which causes a slight impairment of conductivity In atrial flutter however with its less rapid and stronger stimuli the ventricular rate can be reduced only by much larger doses of digitalis and these cannot be administered for any prolonged period of time

There are two methods of procedure quinidine treatment or massive doses of digitalis given in a special way and for a special purpose

Frequently it is possible to abolish atrial flutter with quinidine The method of treatment and the dosage are the same as discussed earlier for atrial fibrillation The danger of peripheral embolism is greatly reduced because atrial contractions in atrial flutter are powerful and thrombi do not occur as often in the appendices as during atrial fibrillation If quinidine therapy fails or is contraindicated because of hypersensitivity or myocardial failure or if myocardial infarction or severe anginal pain exists which makes a quick effect mandatory then digitalis is given The rationale of the digitalis treatment is not to reduce the rate but to transform flutter into fibrillation It has been shown experimentally that an increase of vagal tonus by faradization of the vagus nerve in the neck immediately transforms atrial flutter to fibrillation An attempt is made to accomplish the same result by digitalis via a direct action on the heart muscle and its effect on the vagal tonus For this purpose the administration of digitalis is recommended We have had the best success with digitoxin If five to six tablets of 0 1 mg are given daily fibrillation usually appears on the third or fourth day As soon as this is accomplished it is relatively easy to control the ventricular rate by the

continuous administration of small doses of digitalis. Often sinus rhythm appears spontaneously after the conversion of flutter into fibrillation; if not, it is brought about with quinidine (figure 105).

To be sure, there are cases in which digitalis and quinidine fail to change the existing *atrial flutter*. *If this happens, it is advisable to repeat the same therapy* after an interval of a few months. In our experience the second or third attempt often yields better results.

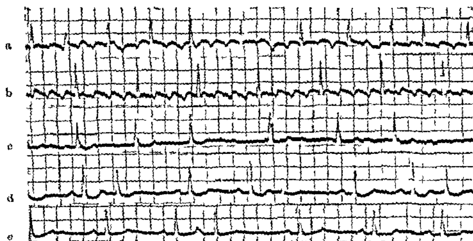


FIG. 105. (a) Atrial flutter with varying A-V block in a 75 year old man; after 0.4 mg of digitoxin was administered daily for two days, a regular 4:1 block appeared (b). Four days later, after the same daily doses of digitalis had been continued, atrial fibrillation appeared (c). Then digitalis was stopped. Four days later sinus rhythm with atrial extrasystoles spontaneously appeared (d). Nine days later the picture is unchanged (e). The RS-T segments are still deformed by the digitalis effect.

Ventricular flutter and ventricular fibrillation are usually terminal events. They may occur during cardiac catheterization and electric shock therapy. Occasionally patients survive such attacks, some of which have been registered in the electrocardiogram. It is interesting that attacks occurred more often in patients with heart block and during treatment with quinidine. Patients have survived attacks lasting as long as six minutes (Schwartz).

In general, standstill of the circulation lasting longer than 3 to 3.5 minutes leads to damage of the cerebral cortex. Therefore, quick action is necessary if *ventricular fibrillation appears. The chest must be opened*, best between the fourth and fifth left ribs, and the heart must be massaged rhythmically at least 40 times per minute. The intracardiac injection of procaine hydrochloride (5–10 ml. of a 1 per cent solution) or application of electric shocks is then used to stop the fibrillation. This procedure has been successful in many instances (Zoll). The external defibrillator is built on the same principle as the apparatus

in use for direct defibrillation of the exposed heart However the countershocks are much stronger (200 to 700 volts as compared to 120 to 150 volts) The duration of the current is about 0 15 second

CLINICAL ASPECTS OF THE TACHYCARDIAS

The tachycardias can be divided into two main groups sinus tachycardias and paroxysmal tachycardias

Sinus Tachycardia

In sinus tachycardia there is a mere acceleration of the normal (sinus) rhythm This is a physiologic phenomenon that occurs after exertion and during excitement In fever the heart rate usually increases 10 beats per minute for each degree rise of the temperature A sinus tachycardia is also found during and for some time after infectious diseases in hyperthyroidism and in cardiac neuroses and many other conditions

While the cardiac rate is only slightly accelerated in some cases (100–120 beats per minute) a rate of 150–180 is attained in others It is very rare for a sinus tachycardia to exceed a rate of 200

A sinus tachycardia is distinguished from other tachycardias by the fact that (1) the tachycardia develops and disappears gradually and (2) any change of position of the patient and even the slightest exertion increase the rate to some extent Regardless of the existing rate sinus tachycardia in hyperthyroidism becomes faster when the patient rises from the recumbent posture a further increase occurs during walking

Drug therapy of the sinus tachycardia has been quite fruitless Even in a tachycardia with a rate of 180 beats per minute as seen occasionally in hyperthyroidism or a cardiac neurosis no improvement is obtained with digitalis or quinidine Only if a sinus tachycardia is due to cardiac failure can the cardiac rate be reduced by digitalis Employment of prostigmine preparations likewise does not yield satisfactory results The most effective measure is the treatment of the basic disease underlying the tachycardia If hyperthyroidism is treated with iodine or thiouracil the tachycardia disappears within a few weeks In recent years it became evident that in some patients a sinus tachycardia may be abolished with Rauwolfia preparations

If the heart is otherwise healthy little damage is done by a sinus tachycardia even when the rate is high but the harm it causes in the presence of organic changes e g coronary sclerosis is considerable

Paroxysmal Tachycardia

The paroxysmal tachycardias are characterized by sudden onset and an equally abrupt termination If the patient has been aware of the tachycardia its sudden onset and the abrupt cessation will have been noted Often however

no sensation of palpitation or other abnormality is experienced with very high rates

Three principal forms of paroxysmal tachycardia are distinguished (1) paroxysmal atrial fibrillation and flutter (2) paroxysmal atrial tachycardia and (3) paroxysmal ventricular tachycardia The last two are also known as essential paroxysmal tachycardias A tachycardia originating in the atrio ventricular node (nodal A V tachycardia) is rare but it is often erroneously diagnosed from the electrocardiogram According to Campbell a supraventricular tachycardia is found in 60 per cent of paroxysmal tachycardias paroxysmal atrial fibrillation in 30 per cent atrial flutter in 6 per cent and ventricular tachycardias in 4 per cent

Paroxysmal Atrial Fibrillation and Flutter These disturbances discussed as permanent conditions in the preceding section are often accompanied by a high ventricular rate Since they begin and end suddenly these conditions belong to the paroxysmal tachycardias The complete irregularity permits the diagnosis of atrial fibrillation without an electrocardiogram The diagnosis of atrial flutter was discussed in the preceding section

The significance and treatment of atrial fibrillation and flutter as permanent states was discussed earlier If short attacks of atrial fibrillation or flutter appear several times a week or daily quinidine sulfate should be given prophylactically One tries as in the case of extrasystoles to obtain success with the smallest possible amounts of the drug Only when quinidine cannot be given or is not tolerated is digitalis administered The result is sometimes similar since the attacks occur less frequently or even disappear completely Often however the attacks persist but digitalis reduces the ventricular rate so much that they are harmless Occasionally digitalis transforms paroxysmal fibrillation into permanent fibrillation which is welcome to the patient and the physician since the patient is no longer in constant dread of an attack The permanent fibrillation is usually easily controlled with small maintenance doses of digitalis

If the attacks occur at irregular and long intervals e g once a month prophylactic therapy is hardly necessary Under these circumstances it is advisable to administer quinidine only during the attacks one tablet of 0 20 Gm is given every two hours until the flutter or fibrillation subsides As a rule only two or three doses are necessary until sinus rhythm reappears If there is hyper sensitivity to quinidine one must resort to digitalis

Essential Paroxysmal Atrial and Ventricular Tachycardia Both types of tachycardia consist of a long series of extrasystoles A tachycardia develops because the interval between the extrasystoles is short

The clinical picture of the essential paroxysmal tachycardias has been studied by numerous investigators all over the world for a long time This has been possible because of its prevalence Atrial tachycardias in particular are very common but only a small percentage ever come to the attention of the physician In the majority of cases the attack is of short duration and is un recognized even by the patient Paroxysmal ventricular tachycardias are rarer but by no means as uncommon as some reports seem to indicate

Fig 106 Atrial extrasystole and a short attack of paroxysmal atrial tachycardia

Fig 107 The beginning and end of a paroxysmal ventricular tachycardia

ELECTROCARDIOGRAM Figure 106 shows a short attack of paroxysmal atrial tachycardia observed in a patient with mitral stenosis (lead II) The sudden beginning and the sudden end of the attack are clearly visible The rate of the tachycardia is 150 per minute A single atrial extrasystole appears in the beginning of the tracing

In Figure 107 the beginning and the end of a paroxysmal ventricular tachycardia are shown the rate is about 200 per minute A single ventricular extrasystole appears after the tachycardia ends

In patients with severe myocardial damage the form of the ventricular beats during ventricular paroxysmal tachycardia varies Similar tachycardias appear following the administration of toxic doses of digitalis in patients with myocardial damage

MECHANISM The same two theories as in atrial fibrillation and flutter are usually advanced in order to explain the mechanism of paroxysmal tachycardias The explanation most acceptable to us is that of a rapid formation of stimuli in an abnormal center

ETIOLOGY In the majority of cases attacks of atrial tachycardia occur in perfectly healthy people showing no evidence of organic heart disease In exceptional cases the attacks are related to excessive smoking pregnancy an injection of adrenalin or the administration of strophanthin or digitalis Ventricular tachycardias also may occur without any symptoms of heart disease but often coronary occlusion or coronary sclerosis is present In rare cases reflexes (paroxysmal tachycardia occurring on swallowing) (Sakai and Mori) or exertion (Scherf) are exciting factors In most of the cases

however the attacks occur without any demonstrable cause Patients with abnormal response to digitalis occasionally have a characteristic type of paroxysmal ventricular tachycardia (see later) and this represents an urgent

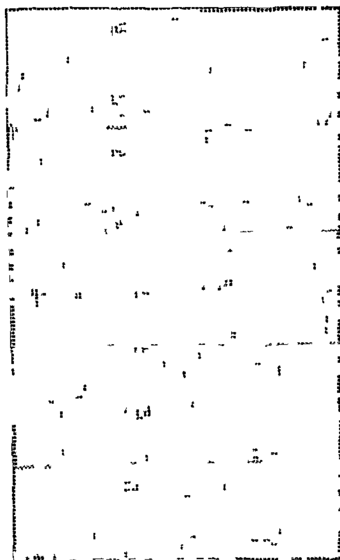


FIG 108 Pre excitation syndrome in a 47 year old man

warning to discontinue the drug Paroxysmal tachycardia has been found at all age and even in infants

About every third patient with the pre excitation syndrome characterized by a very short P R interval and abnormal QRS complexes (figure 108) complains

of attacks of paroxysmal tachycardia Common in these QRS complexes is a slurring or notching of the ascending branch of the R wave The interpretation of this phenomenon as being caused by an accessory A V bundle of conduction (Holzmann and Scherf) is still the most widely accepted one A disturbance of impulse formation in the A V node has been suspected because of misinterpretation of tracings but there is no sound foundation for this assumption (Scherf Blumenfeld and Mueller)

SYMPTOMS Many patients have a fluttering sensation which if accurately described leads to the diagnosis Other patients have palpitation which also should make the examiner suspicious In a large number of cases however only weakness and fainting exist without any unusual sensation in the cardiac area so that the physician who sees the patient after the attack has disappeared has difficulty in reaching the diagnosis Occasionally a patient will describe only a peculiar feeling of anxiety while another has nausea and vomiting (due to hepatic congestion) anginal pain or intense pressure in the cardiac area Meteorism and belching are early complaints In older individuals with atherosclerosis a marked fall of blood pressure with confusion coma or even shock may appear

Of greatest diagnostic importance is the statement that the attacks or sensations start suddenly and end suddenly If the history of the sudden onset and abrupt ending of the attack is elicited the diagnosis is obvious Many patients however particularly those whose hearts are abnormal do not feel the beginning and ending clearly making the positive history alone of value Not rarely the examining physician notes the end of an attack by auscultation but the patient does not feel it has subsided

A peculiar scarcely investigated symptom accompanying various forms of paroxysmal tachycardia is urina spastica the patient reports voiding remarkably large volumes of light colored urine This large amount of urine is passed soon after the onset occasionally during the attack but only rarely after its cessation Since this sometimes unnecessarily alarming phenomenon may occur immediately after the onset of the attack one cannot ascribe it to the disappearance of renal congestion as has been suggested While this phenomenon may be observed in other conditions unrelated to the heart and circulation the finding of urina spastica helps in the differentiation from other forms of tachycardia or palpitation because it is common in paroxysmal tachycardia but very unusual in the sinus tachycardias

Prolonged tachycardias with rapid ventricular action may lead to passive congestion for the same reasons as atrial fibrillation pulmonary edema may even occur Hemoptysis during an attack is not rare and is difficult to explain The temperature is moderately increased presumably due to pulmonary congestion Leukocytosis may be found

The venous pressure is increased the minute volume and occasionally arterial oxygen saturation may fall remarkably The T waves may be abnormal for a few days after a tachycardia (figure 109) (Burak and Scherf)



FIG 109 Paroxysmal atrial tachycardia in a 74 year old man who sought hospitalization for precordial pain Two days after the tachycardia had disappeared the electrocardiogram is markedly altered and shows deep inversion of the T waves in all leads (b) This is not the post tachycardia syndrome described by Burak and Scherf since a normal electrocardiogram was not registered until ten days later The electrocardiogram should have become normal within a few days were the abnormality solely the result of the tachycardia Presumably the patient developed the tachycardia as a consequence of a small myocardial infarction

The size of the heart may decrease during the attack (Scherf and Zdansky) but in a tachycardia lasting over many months with a fast rate both ventricles may dilate and evidence of relative tricuspid and mitral insufficiency may appear.

The manifestations of paroxysmal atrial or ventricular tachycardia differ in each individual case. The course can never be predicted when the patient is seen in the first attack. Even single attacks may exhibit extreme variations with respect to frequency and duration. An attack may recur repeatedly within twenty four hours or the patient may have only one attack in years or *in a lifetime*.

DIAGNOSIS. The rapid, regular action of the heart is easily recognized if the rate is over 150, but with slower rates the diagnosis is often missed without the help of the electrocardiogram. The rate may vary in individual cases between 110 and 250 beats per minute. It is always faster than the existing sinus rhythm. The first heart sound is often accentuated, while the second heart sound may be soft, owing to the diminished output and the fall of blood pressure. In other cases embryocardia is present. If murmurs are present during sinus rhythm they disappear during the tachycardia, since the diastole is much too short to permit their appearance and the systolic output is too small to make a systolic murmur audible. With a heart rate of over 180, a correct count of the pulse becomes difficult.

The frequently made diagnosis of cardiac failure with sinus tachycardia causes the patient and his family unnecessary fright. The attitude of the physician in cases of paroxysmal tachycardias is often wrong, and unfounded alarm more often than not exerts a bad influence on the morale of the patient.

In a paroxysmal tachycardia one should determine first whether an atrial or ventricular type exists. Occasionally this is possible by observation of the venous pulse, since in the ventricular form the atria usually do not participate in the tachycardia and independent slow a waves may be seen in the jugular veins. The differentiation is made easier by the use of the electrocardiograph. On this occasion a warning may be sounded. Many enthusiastic physicians seek to abolish the attack with carotid pressure and often in atrial tachycardias attain success so quickly that no opportunity is afforded to ascertain what type of attack is present. Since the differentiation between the various types of tachycardia has prognostic significance, one should try — if possible — to take an electrocardiogram before therapeutic measures are instituted. Rarely, even ventricular tachycardias are stopped by carotid pressure.

As pointed out before, the rate of the tachycardia has great importance in the clinical picture. In an atrial tachycardia, the atrial contraction precedes the ventricular and aids the filling of the ventricles. If, however, the atrial tachycardia exceeds a certain critical rate (Wenckebach) which usually amounts to 180 beats per minute, diastole is so short that the atria contract while the ventricles are still in systole. Since the atrial systole is superimposed on that of the ventricles, the atria cannot expel their contents into the contracted ventricles and blood moves backward into the venae cavae producing a particularly marked engorgement of the great veins and of the liver.

The appraisal of the clinical picture is easy when the patient has a long history of attacks and can provide information upon all important details. But the problem is more difficult if the patient seeks aid during or after the first attack. Then a decision must be deferred until observation permits a reliable evaluation of frequency, duration and consequences of the attacks.

The same statement is particularly valid in determining the significance of the tachycardia. If the patient reports that the attacks have existed for years and examination reveals nothing abnormal, one is justified in regarding the tachycardia as a harmless disturbance (cf. the statement on extrasystoles). But if patients are seen during or shortly after the first attack, they must be observed for a time even when the first examination is negative, since the tachycardia may be the first and, for a time, the only sign of myocardial disease. All statements made on this subject during the discussion of extrasystoles are applicable here.

DIFFERENTIAL DIAGNOSIS. In most cases it is easy to differentiate between paroxysmal tachycardias and a sinus tachycardia. In patients who do not feel the sudden start and ending, and have only vague symptoms, the diagnosis is difficult unless one has the opportunity to observe the patient during an attack.

Atrial flutter may be difficult to rule out even with the aid of an electrocardiogram.

PROGNOSIS. The majority of attacks occur in healthy persons and have an excellent prognosis. Even if they recur often, the patient is usually able to stop them easily. If he is correctly informed by the physician, any feeling of apprehension that is present may disappear.

The situation is difficult if the attacks respond poorly to treatment or if they last too long or appear too often. In rare cases, cardiac dilatation and congestive heart failure may be caused simply by the tachycardia and death may occur without any evidence of myocardial or valvular lesion (Scherf and Kisch).

The prognosis of ventricular tachycardias is usually considered worse than that of atrial tachycardias. Ventricular tachycardias, to be sure, may also appear for years in patients who show no evidence of myocardial disease, but this is exceptional. Usually organic heart disease, particularly coronary sclerosis, exists; occasionally, as mentioned above, a paroxysmal ventricular tachycardia may be the first sign that a heart lesion is present.

Paroxysmal ventricular tachycardia is an ominous complication of myocardial infarction.

TREATMENT. If the patient is seen during an attack and the diagnosis of an atrial tachycardia is established by means of the electrocardiogram, before the administration of drugs an attempt should be made to abolish the attack by one of the numerous vagal reflexes. If tried with care and patience, they often help, and these procedures have the advantage that the patient can be taught to use them whenever the attack recurs.

At first carotid pressure described as vagus pressure in older literature is applied It is performed in the following manner the patient must assume the recumbent posture because dizziness and faintness may result from carotid pressure The carotid artery is palpated at the level of the thyroid cartilage anterior to the sternocleidomastoid muscle and is pressed toward the vertebra Cardiac activity is simultaneously observed with the stethoscope The amount of pressure exerted differs in every case In some even the lightest pressure suffices while in others the pressure must be strong If several attempts are unsuccessful it is well to repeat the procedure at a somewhat higher or lower level because the site of the carotid sinus varies and pressure at other points is ineffective In a majority of cases the pressure is effective on the right side but pressure is often successful on the left Obviously pressure should not be exerted on both sides simultaneously Many patients soon learn to apply carotid pressure themselves and can thus suppress attacks readily

An attack of paroxysmal atrial tachycardia existed in the patient whose electrocardiogram is reproduced in figure 110 Carotid pressure on the right side was started at the time indicated by the signal The attack ended abruptly (within a few seconds) and was followed by a complete standstill of the heart for a few seconds because the pressure was exerted too long

If carotid pressure is ineffective other vagus reflexes should be tried Some patients can terminate attacks by holding their breath or by a sudden deep inspiration Others succeed by means of the Valsalva experiment that is maximal activation of the expiratory muscles with a closed glottis The patient should be advised to exert pressure similar to the way during defecation Ocular pressure (bulbar pressure) is often effective particularly in youthful individuals The patient looks downward and closes his eyes then gradually increasing pressure is exerted against the eyeball Occasionally bending forward or bending the knees terminates an attack In rare cases pressure on the abdomen or slight mechanical irritation of the skin in the external auditory canal stops the paroxysm Some patients find that touching the pharynx with the fingers provokes retching and abolishes the attack at once

If all these reflexes are tried — which is easily done within a few minutes — the attacks can be terminated in almost 50 per cent of the cases

The drug which is safest and usually successful within a reasonable time is again quinidine sulfate After a test dose shows that no idiosyncrasy exists a tablet of 0 20 Gm is given every two hours day and night until the attack subsides This is usually the case within a few hours although in some cases treatment has to be continued for a few days This treatment is harmless if the patient shows no untoward sign due to hypersensitivity The patient should rest until the attack subsides

If the patient does not tolerate quinidine he should be given digitalis This drug was more widely used in the prequinidine era and nowadays is neglected by many For this treatment as in atrial flutter digitoxin is recommended Digitalis therapy has been very successful for attacks of paroxysmal tachycardia in child

ren The frequently heard statement that digitalis is useless or contraindicated in the ventricular type of paroxysmal tachycardias is not correct

In the majority of cases the attacks need not be abolished immediately No harm is done while waiting for quinidine or digitalis to become effective therefore this method is preferable to those which are speedier but have some untoward and sometimes unpleasant effects

Often an intravenous injection of quinine dihydrochloride or quinidine sulfate is effective and stops an attack of paroxysmal tachycardia immediately (*Singer and Winterberg*) Initially only 0 2 Gm should be injected this amount if not effective may be increased if necessary to 0 4 or even 0 5 Gm on the following day or in the next attack provided the first injection was well tolerated As a rule the attacks cease immediately and usually even during the injection The injection must be given very slowly however and it is not always entirely harmless Quinidine is a cardiac depressant even small doses given intravenously may act adversely on a damaged myocardium Since no one can readily determine whether and to what extent the myocardium is damaged in an unknown patient great caution is advised in the use of quinidine or quinine by intravenous injection Slow infusion with control of heart rate and blood pressure is safer Intramus

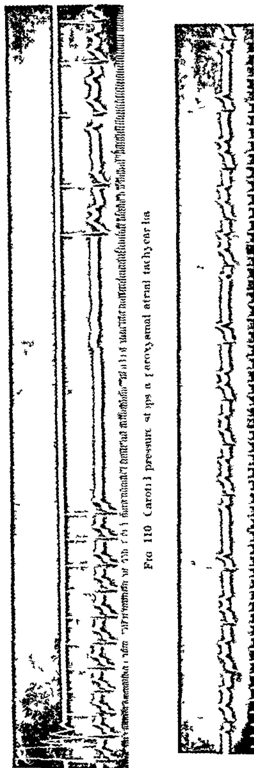


FIG 110 Carotid pressure stops a paroxysmal atrial tachycardia

FIG 111 Periodically dropped beats (*Wenckebach's period*)

cular injections are now possible since preparations are available for this purpose they are devoid of danger in certain cases this route has advantage The injection of a single dose of 0 5 Gm every three or four hours is permissible The same rules obtain for quinidine lactate as for other salts of quinidine

If the patient does not tolerate quinidine or if evidence of heart failure is present digitalis or strophanthin is preferable If quick action is desired the injection of one of the new purified glycosides like Cedilanid (0 4 mg) or digoxin is recommended Still more active is strophanthin which may be given in the dose of 0 25 mg if no digitalis has been administered earlier

Quinidine is superior to digitalis when attacks recur often and prophylactic measures are indicated In this case one proceeds exactly as in the treatment of extrasystoles or paroxysmal fibrillation and seeks to determine the smallest amount effective in preventing the tachycardia

Among the numerous other drugs recommended for the treatment of paroxysmal tachycardia choline or the much more effective derivative acetyl beta methylcholine was found helpful It abolishes the tachycardia in about 85 per cent of the cases The dosage depends upon the weight and age of the patient usually 30 to 40 mg subcutaneously suffice One must have a syringe with atropine ready in case untoward symptoms appear While these are rarely dangerous they are often unpleasant Adenosine triphosphate has been used with success (Komor and Caras) Vagus stimulation by physostigmine often used in the past has been abandoned but prostigmine (0 5—1 0 mg subcutaneously) has less side effects than mecholyl All these compounds are rarely used today

Emetic drugs have also been recommended but the simple suggestion to the patient to induce retching by inserting two fingers very deep into the throat has the same effect without other unpleasant reactions

Pressor amines such as neosynephrine Vasoxyl and Isuprel abolish attack of supraventricular tachycardia but they may elicit dangerous ventricular one The intravenous injection of 0 5 to 1 mg of neosynephrine has been advocated in paroxysmal atrial tachycardias It has been suggested that this dosage be repeated when the blood pressure is normal after 30 seconds however ventricular extrasystoles are common when pressor amines are injected intravenously and they bring danger

It is astonishing what heroic measures and even dangerous drugs have been recommended for this harmless condition which so rarely endangers the life of the patient and for which more conservative methods of treatment usually suffice Apomorphine for instance and even adrenalin were recommended the latter will often abolish the tachycardia but in a certain percentage of cases will cause ventricular tachycardia or even fibrillation

Among the recently recommended drugs magnesium sulfate is often useful Fifteen to twenty ml of a 20 per cent solution are given intravenously No untoward symptoms were seen by the authors in a series of about 60 cases and none have been reported by others injecting this drug in patients with paroxysmal tachycardia Since stronger solutions of magnesium sulfate paralyze the heart

muscle the injection must be given slowly It is contraindicated in patients with a damaged or weak myocardium

In a paroxysmal tachycardia refractory to quinidine in safe dosage and not responding to oral administration of Pronestyl an intravenous injection of Pronestyl may be attempted It should be done very slowly with continuous control of the blood pressure Side effects often appear — as with quinidine — in elderly patients and in patients with a damaged myocardium The necessary dose varies Not more than 100 mg per minute should be injected (Kerry et al) usually 300—1000 mg are needed

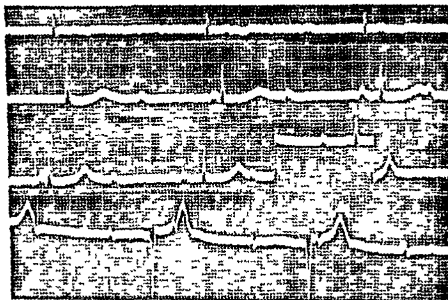


Fig 112 Complete dissociation between atria and ventricles (complete heart block)

Bellet et al noted good results with an intramuscular injection of Pronestyl gluconate or hydrochloride in the dose of 0 5—1 5 gram In this way the severe hypotension which may follow if these drugs are given intravenously is avoided

Of great interest is the employment of potassium preparations in the treatment of paroxysmal tachycardia and extrasystoles The effect of potassium on stimulus formation of the heart has been known since the classical studies of the action of electrolytes on cardiac activity by Loeb Ringer and others It has been recognized that potassium inhibits stimulus formation and in this regard is antagonistic to sodium and calcium The administration of potassium salts by mouth increases the blood level and causes the extrasystoles and paroxysmal tachycardias to disappear (Sampson Anderson) However the dosage is difficult to determine since the effective doses vary in different persons Even in patients with normal renal function dangerous arrhythmias have been observed after oral administration of potassium

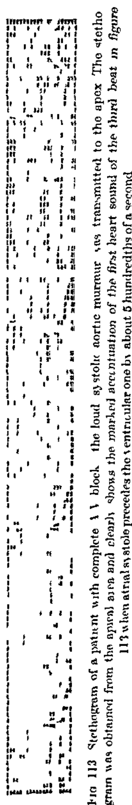


Fig 113 Stethogram of a patient with complete A V block the loud systolic aortic murmur was transmitted to the apex The stethogram was obtained from the apical area and clearly shows the marked accentuation of the first heart sound of the third beat in figure 113 when atrial systole precedes the ventricular one by about 5 hundredths of a second

Two grams are given at the beginning and 1 to 2 grams are repeated every two hours until the attack subsides Potassium iodide is usually recommended Other salts like potassium chloride or acetate are also effective The combination with quinidine has been advised (Stempien and Katz) Following the ingestion of a potassium salt the blood level begins to rise in about 30 minutes and reaches its maximum in two to three hours A blood level of 33 mg per cent of potassium was obtained in this way Sweating and nausea may appear

A rapid intravenous injection of a potassium salt leads immediately to ventricular fibrillation

Conduction Disturbances

Various arrhythmias sometimes of complex structure may be caused by sinoatrial or more frequently by an atrioventricular block Only a few remarks concerning these disturbances can be included in this book For a complete discussion the reader is referred to our textbook on electrocardiography

The simplest and most common conduction disturbance is the prolongation of the PR interval (figures 22 and 94) This causes no disturbance of rhythm and may be suspected only by the presence of a presystolic gallop rhythm Next in frequency is a periodic dropped beat where as in figure 111 the atrial stimuli are conducted progressively more slowly to the ventricle until one atrial impulse is blocked The conduction system recovers the conduction returns to normal or at least is improved for one beat and then the progressive fatigue reappears This condition first described by Wenckebach is now called Wenckebach s period

In the two conduction disturbances described above and in higher degree of partial as well as in complete atrioventricular block (figures 70 and 112) one must at first rule out digitalis therapy as the etiologic agent Digitalis in large quantities is a typical cause of these

conduction disturbances if given when the heart is already damaged even relatively small doses may produce various types of conduction disturbances or even complete heart block If treatment with digitalis did not precede the appearance of heart block then an organic change in the conduction system must be assumed to exist As pointed out in the preceding chapters there are three lesions in which heart block appears very often One is rheumatic fever which seems to possess a peculiar and unexplained affinity for the atrioventricular conduction system The second condition is coronary sclerosis and the third diphtheria It has been mentioned that particularly in an occlusion of the posterior descending coronary artery (right coronary artery) different types of heart block appear Partial and more often complete heart block are also found in congenital ventricular septal defects

Complete A V block can be recognized by auscultation One of the most characteristic signs is the presence of the cannon sounds over the apical area In the presence of a regular heart action one hears periodically a very accentuated often tympanitic first heart sound This does not occur when atrial and ventricular contraction coincide it is present as shown in figure 113 when the atrial contraction precedes the ventricular one by about 5 hundredths of a second For the explanation of this and the discussion of other signs of A V block we refer to our companion book on Clinical Electrocardiography

No specific treatment is necessary in heart block the management of the patient is that of the underlying disease There is only one serious accident in the course of the development of a complete block namely Stokes Adams attacks These were discussed in another chapter where emphasis was directed to the fact that the appearance of this syndrome requires not only a conduction disturbance but also damage to the automaticity of the deeper ventricular centers

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Chapter 30

Peripheral Vascular Diseases

Introduction

Our knowledge of peripheral vascular disease has increased tremendously in the past 40 years For a long time these conditions were investigated and discussed mainly by neurologists (Charcot Erb Weir Mitchell) and were ascribed almost exclusively to a nervous vasospasm In his paper describing erythromelalgia Mitchell called the lesion a rare vasomotor neurosis while Cassirer entitled one of the early monographs on peripheral vascular diseases Vasomotor trophic Neuroses Since then we have learned to differentiate many pathologic entities which can be distinguished clinically by a detailed history and careful examination New methods of examination permit the differentiation between vascular disorders due to organic obstruction and those caused by vasospasm

Recent therapeutic innovations may save limbs from amputation but even at present early lesions are still too often attributed to fallen arches or rheumatism although these errors are less frequent than a few years ago

The peripheral vascular lesions are best classified as organic or functional disturbances The former group can be subdivided into inflammatory processes such as thromboangiitis obliterans or lesions due to tuberculosis typhus syphilis and so forth while another group involves degenerative lesions such as arteriosclerosis Periarteritis nodosa seems to be an allergic phenomenon The functional group includes disturbances such as erythromelalgia acrocyanosis and certain types of the Raynaud syndrome

The lesions resulting from arterial embolism or arterial as well as venous thrombosis form a separate group Only the more common and the more important lesions will be discussed in this book

Symptoms

The frequent combination of inflammatory or degenerative vascular alterations with functional spastic disorders causes diversified clinical pictures The localization the time of appearance of the lesions and many others factors vary according to the nature of the disturbance most complaints of the patients however are the same even when the etiology differs Therefore we shall discuss some of the symptoms at the outset and subsequently add the details characteristic of the different lesions in corresponding sections

Pain This is the most common symptom Often it appears in the calf hip or in the foot during walking occasionally it is also felt at rest and it may come at night particularly if the leg is held in certain positions Sometimes it is constant All transitions between mild gnawing and most excruciating pain are encountered

If pain in the calf appears on walking the patient may be forced to stand still This is known as intermittent claudication The history indicates clearly that the pain occurs after walking a certain distance and disappears a few minutes after stopping Similar to the anginal pain on effort walking for a long time at home even climbing of stairs need not cause the pain This distance may remain constant for a long time and deterioration of the patient s condition as well as any improvement are clearly reflected by shortening or lengthening respectively of this distance

It has been clearly demonstrated that an accumulation of a stable physico chemical stimulus in the tissue spaces (Factor P) the consequence of the lack of oxygen in the muscle fibers is responsible for the pain Possibly the lactate ion is the agent involved in the chemical stimulus (Elliott and Evans)

Intermittent claudication may appear in the absence of vascular disease e g in mitral stenosis or in coarctation of the aorta — whenever that is the difference between the supply of blood to the leg muscles and the needs is disproportionate

In general pain at rest is more unfavorable from a prognostic standpoint than pain on movement The absence of pain during rest does not however indicate an adequate blood supply since pain may be absent in embolism with complete occlusion of the femoral artery and resultant gangrene Pain at rest may indicate impending trophic disturbances and particularly in thromboangiitis obliterans it may be due to an ischemic neuritis

One must differentiate between rest pain in peripheral vascular disease and night cramps which appear in healthy people particularly when toward morning the legs are stretched The mechanism of this pain during which the calf muscles become as hard as a board is unknown Several therapeutic measures have been recommended such as vitamin sodium chloride Benadryl and calcium According to our experience 0 2 Gm of quinidine sulfate taken before retiring helps more than other drugs

Patients with so called restless legs (Ekbom) feel sensations of cold weakness paraesthesias and sometimes pain in the legs and thighs which disappear when they stand or walk The cause is unknown

Fatigue Weakness and fatigue in the limbs are also common and often are the early signs of a disturbed circulation

Paraesthesias and Coldness Often patients complain of numbness tingling pins and needles and other paraesthesias A burning sensation may be present Rarely an unusual coldness is felt in certain parts of the extremities but this finding is by no means characteristic of peripheral vascular disease

In rare cases patients seek advice because parts of the limbs show abnormal discoloration

METHODS OF EXAMINATION AND INTERPRETATION OF FINDINGS

Inspection Inspection of the affected extremities often reveals an abnormal color With widening of the venules in the subpapillary plexus the blood flows slowly and more oxygen is delivered to the tissues so that cyanosis appears Obstruction of an artery in the absence of collateral circulation causes abnormal pallor Increased redness is present if inflammation or other factors cause dilatation of arterioles capillaries and veins A dark violet color is seen in complete or almost complete arterial obstruction with imminent gangrene

These discolorations may be found over the entire extremity in the toes or fingers or in small patches of the shins Differences in the color of the two limbs exposed to the same temperatures are of great importance because symmetrical cyanosis appears under normal conditions when the peripheral vessels dilate abnormally due to a variation in vascular tone and is not necessarily pathologic

The skin may be edematous thickened or thin and atrophic Its texture is often altered The hairs may disappear locally Small ulcers may be present Even muscles may atrophy One should look carefully between the toes for evidence of epidermophytosis

Examination of the nails often reveals trophic disturbances The normal longitudinal ridges are increased and transverse ridges appear The nails may become discolored and may loosen from their bed they may grow slowly or stop growing altogether

Palpation Temperature of the skin is estimated with the palm or the ulnar surface of the examiner s hand He should test the extremities after they have been exposed for 10 to 15 minutes to room temperature The finding of an equally cool skin over both extremities is without great importance because this may be normal but even small differences between the two sides tested after sufficient exposure to room temperature have great significance The level at which a difference of temperature begins should be ascertained A slight difference of temperature is often discovered over the knee at a time when no other place shows significant change A temperature difference of as little as 0 5 C can be detected by palpation Sometimes the affected leg is warmer than the healthy one or the more affected leg is warmer than the less involved one The local temperature is lower when there is perspiration sometimes the more affected limb sweats less profusely than the healthy one

If blanching of a circumscribed area e g the ball of the toe is caused by pressure of the finger normally the ischemic area rapidly becomes perfused again when the pressure ceases The slow return of the color is occasioned by diminished flow of blood while a more rapid flow or increased pressure in the vessels particularly in the venules may cause an acceleration It is true that a prompt return to the previous color may be seen even if circulation in a deeply cyanotic leg i

arrested completely slight differences on the two sides however are important for they are early indications of an abnormality in the circulation This test gives the best results when performed with the involved extremities slightly elevated

Examination of the pulsation in the arteries of all four extremities is the next step In the arms one examines the subclavian and axillary arteries the brachial radial and ulnar arteries at the well known areas

In the lower extremities the femoral artery is palpated at Poupart s ligament midway between the symphysis and the anterior superior spine of the os ileum and followed to the triangle of Scarpa The popliteal pulsations are examined best with the patient prone and the leg slightly flexed at the knee In obese patients the popliteal pulsation is recognized only with difficulty The dorsalis pedis artery *is palpated on the dorsum of the foot between the proximal ends of the* first and second metatarsal bones and lateral to the tendon of the extensor hallucis longus muscle A search for the pulsation of the posterior tibial artery is made behind and a short distance from the internal malleolus

Occasionally pulsation of the two last named arteries is not found on one or both sides in normal people The location of the vessel may vary The dorsalis pedis artery runs a different course over the dorsum of the foot in about 8 per cent of cases Statistics indicate that the artery is absent in about 4 per cent of people bilaterally and in 12 per cent on one side only Variations in the course of the radial artery are even more common

In some patients vascular spasm makes an arterial pulse imperceptible Therefore before it is declared absent it has been recommended that the arteries be palpated shortly after the patient has taken a tablet of nitroglycerin Sometimes the vessels feel sclerotic and do not show pulsations because of deposits of calcium in their walls They are however patent In order to avoid confusing the patient s pulse with the pulse in his own fingers the examiner should palpate the patient s radial pulse at the same time

Although the finding of slight differences on the two sides is important for the diagnosis the occurrence of unilateral variations is so common that no diagnosis should be based on the absence of a pulsating dorsalis pedis artery or an absence of pulsation of the posterior tibial artery on one side alone

Some patients have no pulsation for years in an artery owing to vascular disease but they have no complaints In such instances the arterial obstruction is fully compensated by collateral circulation On the other hand severe trophic disturbances and even gangrene of the toes may appear with the pulse palpable in all major arteries in a limb This happens when the process involves arteries lying distant from those palpated

The following is a useful test for discovering obstruction of the ulnar or radial arteries The patient is asked to close his hands as tightly as possible in order to squeeze the blood out of the palm The ulnar and radial artery are then compressed and the patient opens his fist The pressure on these arteries is released one after the other and the return of color is noted An occlusion of the ulnar

artery for instance is diagnosed if the color does not return with the release of compression on this artery but quickly returns when the pressure on the radial artery is released (Allen) At the same time as the pulsations are felt an attempt is made to determine the condition of the arterial walls

If a distinct pulsation is elicited from the dorsalis pedis artery it should be determined whether or not the pulsation disappears when the leg is elevated from the horizontal toward the vertical position Normally the pulsation should persist at least until an angle of 45 degrees is reached Often it is found in all positions If elevation of the leg to less than 45 degrees causes the pulsation to vanish the existence of organic arterial disease in the lower extremity may be suspected

Blood Pressure The results of palpation can be supplemented in some cases by the measurement of the blood pressure If the blood pressure cuff is placed on the thigh and the pulsations are palpated in the dorsalis pedis artery normally the blood pressure in the lower extremities at least equals the arm reading and usually exceeds it In pathologic processes involving the large arteries of the lower extremities the blood pressure may be much lower on the affected side

Color Changes with Change of Position Of great value is the observation of color changes of the skin after change of position of the leg (Buerger) The patient lies on his back and exposes his legs to the room temperature for about 10 minutes Then he lifts both legs to an angle of 60—90 degrees and maintains this position for about 2 minutes Simultaneously the patient is requested to perform plantar and dorsal flexion of the foot and toes The legs of the weak patient should be supported by the examiner during the period of elevation Under pathologic conditions marked pallor appears over the entire foot or parts of it and here again differences on the two sides have great significance The pallor is noted more often on the plantar surfaces than on the dorsum of the foot Subjective complaints are usually absent although pain occasionally appears If the patient remains in this position for a longer time small red patches may appear amidst areas displaying cadaveric pallor The patient then assumes a sitting position with the legs hanging down Under normal conditions within five to ten seconds the feet become flushed With obstruction of the arterial blood flow the flush appears irregularly and tardily Due to this delay the color is intensified and may be a very bright pink

If such pink areas are rendered ischemic by means of momentary finger pressure subsequently they redden with extraordinary rapidity in comparison to the healthy side The presence of an enormous acceleration of the blood stream may be deduced from the light red color and the rapid disappearance of any anemia produced by pressure

As a rule these changes indicate structural alterations of the arteries but they are also observed in conditions with an abnormal vasomotor tonus

Filling Time of Veins If the legs are elevated the veins on the dorsum of the foot collapse If the patient sits with the legs hanging down the veins refill as greater arterial pressure and arterial blood flow returns The return of venous

filling under normal conditions requires less than 10 seconds A prolongation of the venous filling time indicates obstruction to the arterial blood flow

Reactive Hyperemia This examination may be supplemented by the reactive hyperemia test After being kept in a warm bath for ten minutes the extremities are dried and maximally elevated until some blanching occurs The remaining color is removed by massage While the extremity is still elevated a cuff high on the upper arm or thigh is quickly inflated above the systolic pressure The compression should be maintained for about five minutes — this time is shortened only in patients in whom arterial thrombosis threatens During the period of interruption of blood flow the extremity is kept in the warm bath maintained at a temperature of 35—40 C in order to avoid vascular spasm At the end of the five minute period the extremity is dried and the cuff is deflated The time elapsing until the flush begins to appear is determined and one observes whether it is symmetrical in all parts of the extremity The flush — the reactive hyperemia — normally appears in about five seconds Under abnormal conditions it is delayed even to more than one minute in small or large areas of the leg and appears in some areas earlier than in others The color changes are similar to those seen in the test with elevation of the legs The vasodilatation is due to slowly diffusible substances formed during the arrest of the circulation

With marked diminution of cutaneous blood supply disturbances of sensation are commonly found

The investigations just mentioned can be performed by every physician without the aid of special instruments and often suffice to indicate the presence and extent of a disturbance in the arterial blood supply to a limb These results can be supplemented by a series of other examinations

Oscillometry With this method the pulsations of the arteries lying under the cuff are transferred to an instrument and produce according to the pressure in the cuff corresponding movements of a pointer These movements do not occur when the underlying arteries fail to pulsate This may be due to an occlusion higher up or at the level of the test Absence of pulsation may also be the result of great rigidity of the arterial walls Therefore an artery may not pulsate although its lumen is patent The collateral circulation is not shown by this test The blood supply to an extremity may be adequate in the absence of oscillatory pulsations in fact oscillations in the legs may be missed in some patients who have remarkably few complaints and only a few other signs of abnormal blood supply The condition of the patient may undergo marked improvement without any increase in the amplitude of the oscillations

Conclusions drawn from the absolute size of the oscillations are of no value because they vary in the same areas in different individuals Even in healthy subjects oscillations on both sides may differ Different results are obtained at different times of the same day even when the same area is examined The size of the oscillations depends upon many factors other than the state of the wall of the examined vessel owing to the existence of many variables Even differences on the two sides can be evaluated only if they are marked

In view of these difficulties it has been proposed that in cases of peripheral vascular disease in the lower extremities the excursions with the cuff just above the ankle be compared to those obtained when the cuff is just above the wrist If the reading of the lower part of the leg is used as a numerator the ratio under normal conditions is at least 1 0 that is the oscillations in the lower part of the leg are at least equal to those in the lower forearm If the ratio is lower than 1 0 a peripheral vascular disease involving the lower extremity is present

If conclusions are drawn with caution oscillometry is valuable Often it helps to demonstrate the site of an embolic or thrombotic occlusion and it reveals pulsations of large arteries where pulsations of peripheral arteries are missing

Measurement of Temperature Of value in estimating the progress of peripheral vascular disease and indispensable for the estimation of vascular spasm is the measurement of the temperature of the skin with the aid of a skin thermometer or a thermocouple

The limbs to be examined are exposed to room temperature of 20° C for about 20 minutes A higher temperature should be avoided because even in the presence of peripheral vascular disease the skin readily reaches the temperature of the room Under normal conditions in a cool room (16—18° C) the fingertips are rarely under 20° C while in a warm room (20° C) they are around 32° C Here again differences on the two sides are very important The normal skin temperature varies Usually it is lower in nervous patients because of perspiration

In a large series of observations it was found that normally the temperature of the skin of the arms is slightly above 32° C and 1 to 2 degrees less in the lower extremities Variations from these figures are encountered

The differences on the two sides have greater importance than absolute values since variations are great even in the healthy Differences found in the normal leg in different persons may amount to 8° Still more valuable is information about changes of temperature after maximal vasodilatation and after abolition of any vasospasm present

Vasodilatation Vasospasm disappears in deep general anesthesia following paravertebral block peripheral nerve block after the consumption of large quantities of alcohol the administration of nitrites and in the lower extremities following spinal anesthesia The safest and best way to relieve vasospasm is to bathe the two extremities not under examination in water of about 45 C This simple method usually suffices in patients with unusually high vasomotor tonus however at times no effect is seen Under normal conditions the skin temperature over the toes after vasodilatation will approach the temperature of the body and it is always higher than 31° C The vasodilatation that results from warming distant parts of the body is not caused by a reflex mechanism it is due mainly to warming the vasomotor centers by the blood flowing to them from the bathed parts of the body (Pickering) This simple test is also preferable to measurement of the skin temperature before and after induced fever by the injection of typhoid vaccine or in a sweating cabinet Another method widely used is the

peripheral nerve block e g blocking of the posterior tibial nerve by an injection of novocaine behind the internal malleolus for the diagnosis of lesions of the toes

With these methods the degree of vasoconstriction is estimated furthermore the presence of an early organic occlusion is detected if the temperature does not rise sufficiently Finally the capacity of vasodilatation is estimated in order to ascertain the advisability of operative intervention on the sympathetic nervous system If the temperature does not go higher than 28 C sympathectomy is not recommended

Histamine Test On the basis of investigations by Lewis histamine injected intradermally *was recommended as a test for the vascularization of the skin* (Starr) The skin is cleaned and a few drops of 1 1000 solution of histamine acid phosphate are applied to the spot to be tested *If the skin is pricked with a needle* through the histamine solution without causing bleeding a wheal surrounded by a red flare appears within five minutes

Under pathologic conditions with impairment of blood supply the wheal is reduced in size delayed in appearance or may be absent If the wheal is absent the blood flow is reduced to a minimum or arrested and gangrene is imminent A moderate decrease of blood flow has no influence on the outcome of the test *If the test yields an abnormal result the circulation is definitely affected* The test has proved particularly useful for estimating the viability of tissue

The intradermal injection of 0 2 ml of histamine solution has the same effect

Roentgenography An x ray film of the leg may confirm the diagnosis of an arteriosclerotic vascular disease through the discovery of lime salt deposits in the vessel wall But medial sclerosis is often present for many years in the leg arteries without any signs of peripheral vascular disease being evident Positive x ray findings are observed even in 40 year old patients without complaints and without evidence of peripheral vascular disease Calcification of lower extremity vessels *is found in 65 per cent of men and 28 per cent of woman over 50 years of age* Mural calcium deposits in the arteries of the legs do not indicate narrowing of the arterial lumen Therefore the discovery of such deposits has dubious value in diagnosis and in evaluating the degree of the lesion Different x ray patterns of the calcium deposits are observed in medial sclerosis as compared to atherosclerosis (Lindbom)

Angiography Visualization of the arterial vascular tree after intra arterial injection of some radiopaque substance *can furnish worthwhile information* if carried out by experienced physicians The same holds for venography *Complications resulting from the injection may occur* even thrombosis leading to gangrene complications may be caused by sensitivity to iodine The test should be performed only under exceptional circumstances such as preoperatively in the Leriche syndrome

Other Tests Examination of the skin capillaries under the microscope does not supply much information that cannot be secured by other methods The blood supply to the skin is also estimated by intravenous injection of fluorescein and the study of the skin with the aid of a special long wave ultraviolet light in

a dark room The use of infrared photography is limited largely to the discovery of subcutaneous veins not visible on mere inspection

THROMBOANGIITIS OBLITERANS

Among the occlusive peripheral vascular diseases thromboangiitis obliterans shares first place with peripheral atherosclerosis These conditions together comprise almost 95 per cent of peripheral vascular lesions

The involvement of arteries and veins together was recognized as characteristic of the disease as early as 1878 (Winiwarter) The condition was described in great detail and was named by Buerger

Incidence

The disease usually occurs in young males The incidence in females is estimated to run about 1 to 2 per cent of that of males Until a few years ago only 22 instances in women had been reported (Collens and Wilensky) It seems that this disease is becoming more uncommon Allen Barker and Hines found an incidence of 1 5000 in Rochester Minnesota residents

Thromboangiitis obliterans occurs at practically all ages It has been observed in patients of 15 years one patient was 79 years old A majority of those affected are between 30 and 50 The disease has been reported in brothers

A peculiar susceptibility of the Jewish race was reported It is certain that the disease has been observed in most races and is common in Japan The full blooded Negro has been said to be free from the disease

Etiology

The cause of the disorder is unknown Infection was considered as the most likely etiologic factor since inflammation is always present (Buerger) This conception received support from reports of the successful transmission of the condition by transplantation of a resected involved superficial vessel A variety of microorganisms have been found in the lesion but these reports remain unconfirmed

Injuries of the tissues as a result of exposure to cold have been considered an etiologic factor Since the disease is usually seen in heavy cigarette smokers tobacco with its numerous active constituents as well as cigarette paper was supposed to be responsible While smoking definitely aggravates the condition no proof is available to show that it produces the disease thromboangiitis obliterans also occurs rarely in non smokers

Allergy to tobacco to proteins derived from fungus infections or to ergotism from rye were also blamed Typhus infection has also been considered responsible

The relative immunity of women suggested the presence of estrogenic hormone as a protective factor and treatment with estrogens was recommended on this basis (Snapper)

Pathology

For the most part the disease involves the vessels of the lower extremity Involvement of the arm vessels is less common However the process has been found in the coronary arteries the cerebral vessels gastric and mesenteric arteries Many patients with thromboangiitis obliterans die from coronary thrombosis but usually coronary atherosclerosis is found at post mortem

The pathologic findings are characteristic Segments of arteries and veins are enmeshed in fibrotic tissue The arteries are occluded by fibrous tissue which because of recanalization presents a cribriform appearance Thrombi develop in both arteries and veins The nerves are also included in the fibrotic mass

The process often begins as a migratory phlebitis If an artery becomes involved lymphocytes and leukocytes infiltrate all three layers of its wall Intimal proliferation appears early and secondary thrombosis may follow The artery however is often occluded by intimal proliferation alone In the veins only thrombosis is found Giant cells appear and recanalization progresses slowly The nerves show an ischemic neuritis Wallerian degeneration and evidence of lymphocytic infiltration (Barker) occur The nutrient vessels of the nerves are thrombosed

The disproportion between the extensive occlusion of the large main arteries and the trifling nutritional disturbances is astonishing Even occlusion of the femoral artery is not regularly followed by gangrene (Jaeger)

Symptoms and Signs

Migratory Phlebitis Some of the earliest symptoms are provoked by the migratory phlebitis The incidence of this phenomenon is estimated at 70 per cent although some find it in only 10 per cent of their cases (Telford and Stopford) We noted it in about 20 per cent of our material Inquiry should be made about red painful areas on the dorsum of the foot particularly in the vicinity of the ankles or the lower leg as well as on the lower arm Usually nonvaricose cutaneous veins are affected Pain redness and tenderness are found Slight malaise and a little rise of temperature are present Often a portion of the vein about 2 to 4 inches in length is involved In some cases *however the inflamed* area is smaller and confusion with erythema nodosum or erythema induratum of Bazin occurs The period of acute inflammation lasts about 10 to 12 days and is followed by brown pigmentation One gains the definite impression that the adventitia and the neighboring tissue participate in the inflammatory process

Whenever a migratory phlebitis appears it should arouse the suspicion that a thromboangiitis exists or is developing thereby requiring a careful examination of the peripheral arterial circulation

Pain One of the earliest symptoms is pain In general it is more severe than the pain in atherosclerotic peripheral vascular disease but all degrees between mild pain and excruciating agony are encountered Often the pain appears for the first time after exposure to cold

Intermittent claudication is found in 98 per cent of cases (Goldsmith and Brown) It is felt not only in the calf but also in the foot This pain is not knife like rather it resembles a cramp As in angina pectoris which has the same mechanism the pain often occurs after progressively shorter intervals and lasts longer after cessation of activity Rest pain may be due to impending trophic disturbances such as ulcers or gangrene The rest pain is caused by the arteritis and phlebitis as well as the concomitant inflammation in the surrounding tissue It is also a result of the involvement of the nerves so called ischemic neuritis The latter condition in particular causes pain of unusual intensity The sharp shooting lancinating pain is felt in the whole extremity The patient may consume large quantities of narcotics without much benefit Lack of sleep and lack of food cause rapid loss of weight There is no satisfactory treatment for this type of pain *although even chordotomy has been performed for its relief* It is a difficult task to bring the patient through this period occasionally possible only by the repeated assurance that the pain is of temporary character It may last however for many months and has even driven patients to suicide

Occasionally the pain due to tissue dystrophy is partly relieved when the *leg* is kept down *Patients may sit day and night on the edge of the bed* holding the involved foot (which is crossed over the healthy leg) in their hands massaging it and letting it hang down from time to time This ischemic pain is often aggravated by coexistent vascular spasm initiated by the involvement of the adventitia and causing irritation of autonomic nerves the spasm is accompanied by blanching *If the tests described above show that spasm is responsible to an* appreciable degree its abolition brings quick relief

Other Symptoms and Signs Heaviness and weakness in the legs as well as paraesthesias are early symptoms

Edema is caused by increased venous pressure and damage to the capillary endothelium In some cases ulcers and gangrene appear in or between the toes early in the process

The signs of arterial obstruction discussed on the preceding pages are observed on examination At the beginning and sometimes persistently, the process is unilateral Femoral pulses may be absent in patients who come with trifling complaints If the interosseal and digital arteries alone are involved the peripheral pulses obtained at the usual places may be normal Fungus infections cause early complications and should be searched for assiduously Occasionally the arm arteries are also affected — cases are known in which amputation of all four extremities was necessary However if the upper extremities are affected it is rarely necessary to amputate more *than a finger*

The appearance of symmetrical vascular changes in the arms may simulate a Raynaud like picture Among 389 cases of thromboangiitis obliterans the legs alone were involved in 74 per cent both arms and legs in 24 per cent and the arms alone in only 2 per cent (Brown)

Fever may be present The sedimentation rate is usually *increased*

Course

The course of the disease varies Progress may be very slow or stormy Some cases manifest no more symptoms than those of recurrent thrombophlebitis and the arterial involvement is discovered only by careful examination These patients have no other complaints during a long period of observation In some who complain of intermittent claudication years elapse between exacerbations With canalization and development of sufficient collateral circulation symptoms may even gradually disappear In other observations the advance may be rapid and *the first episode may lead to gangrene Sometimes the process is* fulminating from the beginning leading within a few days to the purple discoloration of developing gangrene

The course is unpredictable but *with modern treatment the necessity* for amputation is much rarer than formerly This is partly due to the fact that amputation is performed much later than previously We have learned that despite *very advanced nutritional changes* remarkable improvement *may appear* suddenly even when amputation seems inevitable

Differential Diagnosis

This may offer great difficulties particularly in men over 50 when the condition must be distinguished from atherosclerosis The presence of a *migratory phlebitis is of diagnostic importance The discovery of calcified vessels* in x ray pictures of the legs has small value in patients over 50 because it is so common in the average individual of this age without peripheral vascular disease *It has been claimed that arteriography shows a different pattern of anastomoses* in thromboangiitis obliterans as compared with atherosclerosis (Edwards)

Confusion of thromboangiitis obliterans with ingrown toenails occurs and may lead to unnecessary and detrimental operations

The differentiation of the condition from Raynaud s disease or peripheral embolism is usually easy

Treatment

Treatment cannot be directed against the etiologic factor of thromboangiitis obliterans As soon as the disease is recognized by the discovery of a disturbed peripheral blood supply active therapeutic measures should be undertaken to prevent further damage to the peripheral circulation and to improve collateral circulation It seems that in most cases careful observation of the measures discussed below can prevent gangrene and amputation Even if new exacerbations cannot be prevented with certainty much can be accomplished

Hygienic Measures Since the arterial blood supply to the tissues is diminished the first efforts should be directed against any increased demands if these demands cannot be fulfilled nutritional changes are the consequence Rest is therefore necessary Local heat which was widely used in the past is strictly *forbidden* With *increased* tissue temperature the metabolism and therefore

the oxygen requirements rise This is not compensated by an increased speed of oxygen dissociation from hemoglobin with the result that gangrene may follow the application of heat Rest is indicated in the presence of wound, gangrene or the appearance of rest pain Since trauma and infection impose greater demands for blood and the tendency to venous thromboses they should be carefully avoided Fungus infections in particular are responsible in many cases for the aggravations and complications in the disease Living in a warm climate is beneficial

Antibiotics are given for streptococcus infections and penicillin is injected if need be even intra arterially (Glasser et al) If fungus infections are present the patient should bathe his feet twice daily for thirty minutes in a 1 3000 solution of potassium permanganate or soak them in Dakin s solution or in a warm boric acid solution The same treatment is used if gangrene or ulcers exist The resistance of the body to infections and sepsis is much greater in thromboangiitis than it is in peripheral atherosclerosis

Without the indications for bed rest mentioned above the patient may be up and about although too much walking should be discouraged With severe pain the dependent position of the leg may bring relief This position however should not be maintained too long otherwise the formation of edema is favored which also impairs tissue nutrition

If patients walk more slowly than they usually do the pain appears either much later or not at all

Talcum and dusting powders should be used freely to keep the feet dry

The shoes should be comfortable and should be changed often The socks should be made of soft wool Bed socks are of value Constricting elastic bands (garters) should be avoided The nails should be carefully trimmed and meticulous care should be taken to avoid every injury The nails should not be trimmed too short and the cutting should be straight across In order to avoid ingrown toenails an important complication capable of producing serious consequences the patient or physician should file the surface of the nail of the big toe in order to relieve lateral pressure

The feet should be bathed at least twice daily they should be dried carefully with particular attention paid to the interdigital spaces If the skin is too dry lanolin should be used if perspiration exists talcum powder should be applied often The legs and feet should always be kept warm

Operative removal of bunions is prohibited for corns an ointment containing salicylic acid may be used but with great caution A callus should be treated with sandpaper The patient should not sit with his legs crossed Overeating should be avoided but no special diet is necessary

A fundamental rule in the therapy of thromboangiitis is strict abstinence from smoking The greatest stress must be laid on this advice It is a repeatedly confirmed fact that smoking even one cigarette not only increases blood pressure and heart rate but lowers skin temperature as well While there is no convincing proof that tobacco is an etiologic factor there is no doubt that smoking even a

few cigarettes may cause a severe relapse it may prevent wounds from healing and may cause new areas of gangrene to appear One observer followed 100 patients with thromboangiitis obliterans who stopped smoking for over 10 years The disease was completely arrested *in all cases* (Silbert) *It does not* suffice to tell the patient not to smoke The dangers of smoking must be explained in detail to the patient and he should be informed that gangrene and mutilating operations are avoidable only if smoking is completely omitted The detrimental effect of tobacco in peripheral vascular disease was known for many decades but the importance of this factor in the treatment of thromboangiitis obliterans has been appreciated only in the last 25 years

Heat Treatment The damage resulting from exposure to cold and the benefit of warm temperature was recognized early and led to the application of warmth by different means (diathermy sitz baths) The warm foot bath as well as the contrast bath and heat cradle were widely used although often with detrimental effects The damage done by heat applied directly to undernourished tissue was explained above It is far safer to attempt to dilate the vessels to stimulate and improve collateral circulation in the legs by immersing the healthy arms up to the elbows into water at 40 C or more simply by applying a heating pad to the abdomen

Active Vascular Exercise In order to improve collateral circulation Buerger introduced vascular exercise It has been widely used in the past The legs are at first elevated to an angle of about 60 degrees and kept in this way two to three minutes until blanching occurs This is best done if the back of an inverted chair is used for support The patient should then dangle the legs for three to five minutes until maximal flushing develops This procedure is repeated five times and at each of three or four daily sessions These exercises as well as the procedures discussed in the two following paragraphs are contraindicated if an infection or an open wound exists The value of this therapy has not however been proved

Passive Vascular Exercise Another method of physical therapy is called suction and pressure treatment The involved extremity is put into a hermetically sealed boot Alternately high and low pressure is introduced within the boot for the purpose of expelling blood from the vessels with the high pressure and drawing blood into the dilated vessels during the low pressure period Similar methods of treatment have been known for more than a century but recently were revived and improved The original very enthusiastic reports have given way to some skepticism concerning the value of this treatment Here again there is no proof of an improvement of blood flow

Based on the finding that venous compression if sufficiently prolonged causes a reactive hyperemia similar to that of arterial occlusion intermittent venous occlusion by means of a special apparatus was recommended for treatment of peripheral vascular disease Success with this treatment has been reported repeatedly although some authors are somewhat skeptical We find *no* advantage in using any of these methods in the treatment of thromboangiitis obliterans

Drugs. This treatment is often neglected in favor of the methods discussed above. Caution is in order. If strong general vasodilators are used, the blood flow in the diseased extremity may diminish for obvious reasons.

Papaverine, one of the most active vasodilators, is hardly ever used in the treatment of peripheral vascular disease. The vasodilating effect is slight if the drug is given orally. Intravenous and intramuscular injection are more effective but the vasodilatation is evanescent.

Much too rarely used, in our opinion, are preparations of theobromine or theophylline. The vasodilating effect of these agents is small if given orally in the usual doses, but they are powerful and the action is prolonged when given intravenously. We feel that the most active drugs are aminophylline (theophylline with ethylenediamine) and theophylline sodium acetate. We prefer the latter because no reactions follow its intravenous administration. Five to ten ml of a 5 per cent solution are injected intravenously every day for 15 days. The injection is performed slowly. The improvement in some cases is astonishing. The patients can walk farther without pain in the calves, the leg feels warmer and wounds heal faster. The series of injections can be repeated whenever indicated. Apart from rare instances of idiosyncrasy, no untoward results are seen even from prolonged treatment. One begins with 5 ml and gives 1 more ml every day. If the full dose of 10 ml stimulates the patient too much, 6 or 8 ml are given. If theophylline sodium acetate is not available, aminophylline in the dose of 0.25 Gm is injected very slowly.

Between the series of injections, suppositories containing aminophylline may be used, one suppository of 0.5 Gm once or twice daily.

Many other measures are recommended but are much less useful.

Since spontaneous gangrene of the extremities was believed to be associated with an increased viscosity of the blood, infusions of sodium chloride to decrease this effect have been advised. Later, the injection of 150–300 ml of a 5 per cent sodium chloride solution was recommended for the same purpose (Silbert). Two to three injections are given weekly and continued for many months. This treatment temporarily met with great popularity but has been abandoned in most places. Chills, hepatitis, and venous thrombosis sometimes follow the injections.

More success is obtained with injections of foreign protein, particularly typhoid vaccine. Triple typhoid vaccine (Lederle) or typhoid H antigen (Lilly) are used. The doses must be small in order that chills or a steep rise of temperature with accompanying vasospasm be avoided. The first dose is around 5 million organisms; this dose is increased slowly in the following injections, which are given every third to fourth day. The injection is repeated only if the effects of the previous one have disappeared entirely. The use of larger doses has been followed by arterial thrombosis, presumably caused by vascular spasm during the chill (Allen and Smithwick).

Choline derivatives were also employed as vasodilators. The original method of administration by the intravenous route has been abandoned because too

many untoward effects were noted Iontophoresis with acetyl beta methyl choline chloride (Mecholyl) has been used in some peripheral vascular diseases with little success Histamine iontophoresis has also been tried Priscoline (tolazoline) an adrenergic blocking substance is often used but this may cause cardiac pain

Repeatedly the administration of muscle extracts and of insulin free pancreatic extract has been recommended The best known preparation Depropranex is given intramuscularly in doses of 2 ml twice weekly Proof that this treatment is beneficial however is still lacking in our opinion

Based on reports of vasodilating action of estrogens and the observation that thromboangiitis obliterans is rare in women the use of estrogens was advocated Recently androgens were also reported to be of benefit Here again the opinions of authorities differ Benefit is reported by some no effect by others

Mild adrenergic blocking agents such as Ilidar (azapetine) may yield some effect when vasoconstriction exists Arlidine acts in a similar way

In the treatment of these cases it should not be forgotten that one of the most pleasant remedies for many patients and at the same time a very active vasodilator is alcohol It should be given often During an acute exacerbation with excruciating pain large doses may give more relief than any other drug and may tide the patient over a critical period

Surgical Measures For patients with intolerable pain crushing or blocking of nerves was recommended These procedures do not always help and as was pointed out some of these patients have even required a *chordotomy* as the final possible therapeutic step after all other measures were unavailing

Therapeutic sympathectomy is done only in selected cases It should never be performed following an acute exacerbation or in patients whose complaints are only of short duration One must be satisfied that arterial spasm contributes greatly to the clinical picture before undertaking it However the response to sympathetic block may be poor while sympathectomy helps Block may lead to damage of the cord and nerve roots It helps only for about 8 hours

Resection of the second third and fourth lumbar ganglia provides good results Vascular spasm is eliminated sweating is abolished and the legs become warmer In cases of gangrene it is well to avoid operation There is also no certainty of therapeutic success in intermittent claudication Preganglionic sympathectomy has been recommended as the most beneficial procedure (Adson) The necessity and advantage of this operation in a given case should receive serious consideration This mortality is estimated to amount to about 2 per cent The morbidity after the operation also deserves consideration The tonus of the peripheral vessels recurs after a few months and they show greater sensitivity to the action of adrenalin

In recent years surgical restoration of the lumen of arteries by extirpation of the occluded area and end to end anastomosis has been attempted

Periarterial sympathectomy recommended by Leriche was abandoned when it was shown that the vasocontrictor nerves run with the peripheral mixed nerves and join the peripheral arteries segmentally

ATHEROSCLEROTIC PERIPHERAL VASCULAR DISEASE

Atherosclerosis (arteriosclerosis obliterans senile gangrene endarteritis obliterans) is the most frequent peripheral vascular disease and as pointed out earlier with thromboangiitis obliterans comprises about 95 per cent of all peripheral vascular cases

Peripheral vascular disease of diabetes (diabetic gangrene) is often separated in the discussion of this subject but fundamentally it concerns the same pathologic anatomic subject and the clinical manifestations are identical The fact that the disease occurs in diabetic individuals however is responsible for its earlier appearance the poor tendency to heal once ulcerations are established and the frequency of secondary infection

Incidence

The disease usually is encountered in persons over 50 years of age but it may appear much earlier in diabetics Women with the exception of diabetics are less often affected than men the ratio being about 6 to 1 The condition is often unilateral The arms are rarely involved One third of the patients have hypertension

Pathology

The pathologic changes are those of atherosclerosis with the same manifestations and symptoms as discussed in previous chapters in connection with atherosclerosis in other parts of the body The frequent involvement of the arteries in the lower extremities as compared to the rarity of the condition in the upper extremities has often been the subject of discussion In general the atherosclerotic process increases with the distance from the heart The descending aorta shows more involvement than the ascending aorta the abdominal aorta is even more affected and atherosclerosis is most common in the lower legs This is not due to an increased blood pressure in the lower extremities as was long believed for the pressure differences between the upper and lower extremities are not great The upright posture of man is not responsible because the process is common in animals as a matter of interest the first case of intermittent claudication due to atherosclerosis was described in the horse by a veterinarian

Atherosclerosis of the leg arteries often is very pronounced although the patient is symptom free This is usually explained by the fact that the process has not as yet led to arterial occlusion, if this did happen the occlusion occurred so slowly that adequate time was available for the development of a collateral circulation

Atherosclerosis causes vascular occlusion by fibrosis or by thrombosis which may involve large or small arteries In 90 per cent of amputated legs two or more vessels are occluded

When symptoms and signs of ischemia appear (rest pain pretrophic pain) one or more vessels are completely occluded

Atheromatous debris from atheromatous patches in the aorta may cause peripheral embolism (Flory)

The veins are rarely involved and in contradistinction to thromboangiitis obliterans there is no evidence of inflammation This factor the intimal atherosclerosis and the absence of intimal proliferation permit the histologic differentiation from thromboangiitis obliterans

The clots undergo hyaline and fibrotic changes secondary calcification also occurs in time there is some recanalization The media is often thin due to degenerative processes

Symptoms and Signs

The complaints of the patient and the objective findings are very similar to those of thromboangiitis obliterans The picture is *modified* by the rarity of thrombophlebitis and by the minor role of arterial spasm Presumably this results from the absence of adventitial and periarterial inflammation and the absence of nerve involvement

Intermittent claudication is the most common complaint and often involves only the toe or the heel The pain may appear at night and at rest and may be relieved if the covers are removed and the leg is exposed to the cooler air of the room Rest pain may also disappear if the legs are kept in a dependent *position* Patients often feel better if they walk at night when the pain appears and they are relieved if the upper end of the bed is elevated so that the legs are the lowest part of the body

These spontaneous nocturnal pains should not be confused with the night cramps in the calf that were mentioned earlier

Paraesthesias are often present One of the earliest symptoms is fatigue and heaviness of the legs

Sudden aggravation *occurs* if an arterial *thrombus* forms Under these circumstances the picture varies Sometimes gangrene with intolerable pain may appear within a few days Other patients have redness and swelling of a toe or a part of the foot resulting in the development of an ulcer Sometimes there are no signs of impaired tissue nutrition but intermittent claudication and other complaints increase in intensity

Due to the development of collateral circulation slow spontaneous improvement of the condition is not rare

Even if the involved artery becomes occluded the paroxysms of rest pain particularly at night never reach the severity that characterizes thromboangiitis obliterans In the rare case of extreme vasospasm petechiae develop in the lower leg (Hines and Barker)

The sign are those of arterial occlusion and diminished blood supply to the extremity It is important to realize that patients with atherosclerosis of the leg arteries may complain of intermittent claudication without showing evidence of diminished blood supply in the superficial tissues

Gangrene may appear after a spontaneous thrombosis In most cases thrombosis of a peripheral atherosclerotic artery is the result of the rupture of a giant capillary in the intima as in coronary thrombosis Gangrene often follows the least trauma and infection

Roentgenologic demonstration of lime salt deposits in the vascular wall provides little help for the diagnosis It is sometimes not seen in spite of marked nutritional disturbances resulting from atherosclerosis In many cases it is very pronounced when the arteries are patent and circulation is normal Monckeberg's medial sclerosis does not disturb the blood supply to the tissues In this condition concentric incomplete rings are found while in atherosclerosis diffusely distributed placquelike densities are seen

Clinical Course

All variations are seen Within a few days gangrene may follow thrombosis in a patient without previous complaints in others a long duration of intermittent claudication over many years may be noted without complications or exacerbations Prognosis therefore is difficult In one series of patients with obliterative atherosclerosis of the leg vessels 54 6 per cent died after an interval of three years (Hines and Barker)

If accidental complications such as coronary occlusion or heart failure do not hasten the end progress of the condition may lead to gangrene Arrest of the disease is much rarer than in thromboangiitis obliterans and amputation are therefore more common

The separation of gangrenous parts from healthy tissues often takes many months It is astonishing how painless this is in some cases particularly when dry gangrene develops Cellulitis lymphangitis and other infections are common especially in diabetic patients

The appearance of atherosclerotic disturbances in the arteries of the legs in diabetics has been said by some to be independent of the severity of the diabetes its relative duration and even from therapy while others find it more commonly in neglected cases It appears in diabetics 10 times more often than in comparable age groups of controls

Treatment

The treatment consists of the same general hygiene and the avoidance of injurious factors such as excessive heat and cold trauma and fungus infections as discussed in the section on thromboangiitis obliterans Smoking is absolutely forbidden although abstinence does not prevent progression of the process The use of alcohol is permissible

A daily bath is enforced with cautious drying lanolin is used to soften the skin Corn pads may be worn but no local chemical applications are permissible

Among the various drugs mentioned in the preceding chapter only aminophylline (theophylline) in the form of suppositories and intravenous injections have yielded satisfactory results for us We wish to stress that we do not know of any other medical therapy that is equally efficient

Depropanex given once daily for the first week and then gradually less often has been recommended Its action may stem from its content of adenosine phosphate

The administration of anticoagulants is recommended for 2 to 3 weeks when thrombosis seems to threaten This event cannot however be predicted and the preventive power of anticoagulants appears doubtful to us since vascular thrombosis (like coronary thrombosis) seems often to be caused by rupture of a giant capillary in the atherosclerotic lesion

Blocking of nerves for the relief of pain is necessary much less often than in thromboangiitis obliterans

The value of such various methods of physiotherapy as suction and pressure is even more debatable than it is in thromboangiitis Postural active exercises are recommended

The appearance of gangrene or ulcers necessitates bathing the feet in solutions of permanganate or of boric acid The involved parts are kept dry with a mixture of 20 per cent boric acid and 80 per cent talcum

Opinions concerning the value of preganglionic sympathectomy are more divided than in thromboangiitis obliterans Most observers are opposed to operation since the contribution of vascular spasm to the general picture is small in atherosclerosis Naturally the operation is performed in this disease only if the presence of arterial spasm is revealed by the measurement of temperature on the involved area before and after vasodilatation Gangrene has followed the operation despite the fact that skin temperature rose to 30 C after dilatation Return of vascular tone after operation is common It seems that postoperatively the vessels develop an increased sensitivity to adrenalin

De Bakey et al observed improvement in 85 per cent of patients without gangrene following sympathectomy Even with imminent gangrene extremities could be salvaged Major on the other hand found a significant improvement of intermittent claudication in only 9 of 54 patients following sympathectomy

In patients with intermittent claudication tenotomy of the tendon Achillis has been recommended Boyd et al had a good result in 22 of 24 patients and not one patient was unrelieved The operation is done subcutaneously The rationale is not clear Hamilton and Wilson had the operation performed with success in 4 of their patients

In segmental atherosclerotic occlusion resection of the involved part and replacement by autogenous vein grafts or homologous veins (saphenous superficial femoral) and bypass surgery has been attempted with success (Julian et al)

Mortality from operations is reduced with the use of refrigeration anesthesia

NARROWING AND THROMBOSIS OF THE INTERNAL CAROTID ARTERY

Thrombotic occlusion of the internal carotid artery of atherosclerotic origin is a common condition It has been found in 3 per cent of routine autopsies one observer found 45 such patients within two years The frequency of this condition was first stressed by Moniz et al

Men between the ages of 35 and 65 years provide most examples The patient experiences unilateral frontal headache pain around the eye nausea and vomiting Muscular weakness appears with drowsiness or temporary loss of consciousness or paresis in one arm or one side of the body Temporary hemihypesthesia or paraesthesia occurs as does complete but often temporary hemiplegia

Aphasia occurs In repeated attacks the same pattern is observed Tinitus paraesthesias and unilateral blurring of vision are noted Cataracts develop early total blindness may occur Facial atrophy may develop while convulsions with loss of consciousness and epileptic attacks have also been described The combination of homolateral blindness and contralateral cerebral lesions is characteristic

Palpation reveals the absence of pulsation of the internal carotid artery along the anterior border of the upper sternocleidomastoid muscle and in the fossa tonsillaris But even when pulsations are found the possibility of a thrombus situated higher up should be considered Most often the thrombosis is located at the origin of the artery

Men are more often affected than women The lesion occurs more often on the left side Both carotid arteries may be occluded by thrombi without consequences if the circle of Willis functions well

An arteriogram is rarely necessary and is not recommended because of the dangers involved

The course varies Some patients have only narrowing of the artery with attacks of the above described symptoms and signs coming on repeatedly over a period of many months Others die immediately after thrombosis of the artery

Anticoagulants should be given permanently to patients with incomplete occlusion

In several patients a successful resection of the thrombosed artery and direct anastomosis of the ends was performed (Denman et al Eastcott et al)

The first portion of the carotid artery is second to the abdominal aorta in it liability to atherosclerosis

ARTERIAL EMBOLISM AND THROMBOSIS

Etiology

Embolism of the arteries in the arm or leg occurs most often in patients with cardiac disease In patients with atrial fibrillation the emboli come from thrombi in the atria in one autopsy study it was found that 43 3 per cent of patients with rheumatic heart disease and atrial fibrillation had atrial thrombi (Garvin) Emboli often arise from thrombi in the left atrium e g in the course of mitral stenosis In myocardial lesions they originate from mural thrombi in the left ventricle

particularly in coronary disease with myomalacia and in myocarditis Cardiac disease was present in over 69 per cent of a series of cases with peripheral arterial embolism (Pearse) Emboli also arise from thrombi formed in aortic aneurysms or from atheromatous patches on the aorta

With a patent foramen ovale emboli are transferred into the greater circulation from thrombi originating in the pelvic veins or the veins of the lower extremities (paradoxical embolism) This phenomenon is not as rare as is commonly believed On two occasions one of us saw at necropsy the embolus caught just half way through the patent foramen ovale

Emboli usually impinge where arteries divide particularly at the bifurcation of the common femoral iliac brachial or popliteal arteries Embolism is particularly common in the posterior tibial artery

Additional (secondary) thrombus formation following an embolism is a common event It occurs mostly centripetally and may spread a long distance up the vessel and occlude the important collateral arteries

It is sometimes extremely difficult to differentiate primary arterial thrombosis from embolism If evidence of arterial occlusion appears in a patient with peripheral vascular sclerosis thrombosis is more probable Arterial embolism is more probable in patients with cardiac involvement Arterial thrombosis is occasionally seen in severe infectious diseases which frequently damage the vascular endothelium It is rarely observed following operations

Embolism in bacterial and subacute bacterial endocarditis was discussed earlier

Pathologic Physiology

The consequences of arterial occlusion by embolism and thrombosis depend upon the location of the occlusion and the availability of a collateral circulation The latter will develop easier with young elastic arteries than in peripheral atherosclerotic vessels of the aged

In many cases of peripheral arterial embolism the initial dramatic clinical picture observed disappears completely within a few hours Since the dissolution of the embolus is highly improbable presumably this improvement depends upon the disappearance of reflex arterial spasm which participates in the acute picture

If patent vessels are available effective collateral circulation may develop quickly for ligation of the main artery of a limb may be devoid of serious consequences A radial pulse following ligation of the brachial artery may reappear within a few days Embolism into the arteries of the upper extremities is rarely followed by gangrene

Complete interruption of the blood supply to the muscles leads to their death within 6 to 8 hours while nerve fibers survive for about 12 to 24 hours

Symptoms and Signs

Severe pain develops in many cases There is no certainty that the pain will develop immediately or after a short interval In all probability the original pain

is due to vascular spasm while pain appearing later is caused by ischemia Often the pain is excruciating and requires the administration of large doses of morphine but some patients have relatively little pain or even none at all In one series of peripheral arterial embolisms pain was reported in only 64 per cent of the cases in only 53 per cent did it appear immediately (Rykert and Graham) With the development of gangrene late pain is the rule In another study 59 5 per cent of the patients had sudden pain in 21 7 per cent numbness and coldness appeared suddenly and in 5 7 per cent the lesion was silent Those patients without early pain are in greater danger of losing the limb or a part of it because the situation is not realized at once and treatment is not started Time and again we have observed that the nursing staff paid no heed to the complaint of a patient about moderate pain in the lower leg and the physician was notified only after the lapse of many hours Peripheral embolism is diagnosed earlier if the nursing personnel and physicians are embolism conscious

With the pain or independent of it numbness and tingling with a pins and needles sensation appear in the involved part of the limb The affected limb feels cold

The affected extremities may show a very pronounced initial pallor particularly if there is much arterial spasm The cutaneous veins are empty Cyanosis may be present from the beginning unless the veins are empty Cyanosis together with mottling of the skin prevails in later stages Wheals and blebs may appear within 36 hours particularly when the surrounding temperature is warm

No peripheral pulse is found in the involved area The part feels cold and assumes the room temperature when exposed to it This coldness begins a few inches below the occlusion It should be emphasized that the involved limb may feel warm if it was well covered or if heat was applied to it Oscillometry shows no excursions and permits one to locate the occlusion Muscular paralysis appears within 30 minutes the sensory nerves are disturbed and the reflexes are diminished or absent

Fever with leukocytosis and an increased sedimentation rate appear The patient shows evidence of toxemia

Prognosis

It is estimated that recovery occurs in about 50 per cent of patients with embolism or thrombosis even without surgical intervention Spontaneous recovery was seen in 20 out of 36 cases (Rykert and Graham) of occlusion of the femoral or popliteal artery Owing to the seriousness of the general condition of the patient and the disease responsible for the embolism or thrombosis about 50 per cent of the cases in one series died within one month (Pearse)

Treatment

Opiates must be given to relieve the acute pain The involved extremity is kept warm but the application of heat should be avoided The ingestion of alcohol is useful In order to diminish the danger of secondary thrombosis heparin should

be started immediately Fifty milligrams are given intravenously every 5 to 6 hours

Collateral spasm is combatted by means of vasodilators Papaverine in the dose of 0 03—0 06 Gm is injected intravenously or into the artery of the involved extremity (Leiner) Theophylline or aminophylline is injected intravenously in the amount of 0 25—0 5 Gm

Paravertebral block epidural block or subarachnoid spinal anesthesia are used and often result in marked improvement

In cases without gangrene experience with these conservative measures shows that the results obtained are as good as with embolectomy In many cases however the development of gangrene cannot be prevented with conservative methods and therefore embolectomy will always retain its place Different opinions are expressed on whether the therapeutic procedure should be purely conservative or surgical In our opinion all the conservative measures discussed above should be instituted immediately If there is no sign of resumption of blood flow within six hours embolectomy should be done provided the underlying disease is one in which postoperative survival can be expected

If possible embolectomy should be done not later than 12 hours after the occlusion however successful operations have been performed after 24 hours The chances of full recovery are less with belated performance of the operation since the arterial endothelium is so damaged that arterial thrombosis may develop despite a successful embolectomy The problem is rendered difficult because it is not always easy to locate the site of the occlusion Symmetrical gangrene may be caused by a riding embolus at the bifurcation of the aorta or peripheral embolism in both lower extremities

Since the pioneer work of Key successful embolectomy has been repeatedly performed in every major hospital In one of our observations a riding embolism was diagnosed at the bifurcation of the aorta in a patient with a rheumatic mitral stenosis During the transportation to the operating room the embolus split into two parts and the patient developed signs of an embolism in the popliteal artery of one leg and in the femoral artery of the other The patient was operated on immediately by two surgeons one working on each side and survived the bilateral embolectomy When last seen she was in satisfactory condition and could walk without complaints

Sudden appearance of tingling in an extremity that previously was without sensation may indicate the recurrence of blood flow Observation with the capillary microscope may reveal the presence of a slight circulation and encourage conservative treatment

The opinions about the necessity for administering heparin are divided One group of observers gives heparin immediately another points out the dangers of embolectomy while a patient is under the influence of heparin Furthermore very serious and often lethal retroperitoneal hemorrhages have occurred when sympathetic block is performed during the administration of an

anticoagulant Therefore anticoagulants are only given if one is reasonably certain that no embolectomy will be done

OCCLUSION OF THE MESENTERIC VESSELS

Occlusion of the mesenteric vessels is a relatively common event especially in patients with atrial fibrillation bacterial endocarditis or atherosclerosis It may derive from either embolism which occurs particularly in the two conditions mentioned first or thrombosis Thrombosis is seen in atherosclerosis polycythemia infections and trauma Compression by tumor is also provocative Most frequently the superior mesenteric artery is involved The veins may also become thrombosed

Narrowing of the mesenteric arteries leads occasionally to the picture of abdominal angina the dyspraxia abdominalis intermittens arteriosclerotica of Ortner The pain is periumbilical and appears one to one and a half hours after eating i e at the height of digestion

In a venous occlusion prodromal signs may appear An arterial occlusion starts dramatically

An overwhelming steady and not colicky pain over the center of the abdomen appears and is accompanied by shock and vomiting In some cases the pain is less severe and patients with small emboli may survive at times without surgical intervention Infarction is not invariable Occasionally the symptoms are those of an acute intestinal obstruction or peritonitis Constipation or diarrhea is found Leukocytosis nausea and vomiting appear When serosanguinous fluid is found on peritoneal tap exploration is indicated (Mersheimer et al) The mortality even with an operation performed in time is about 90 per cent

OCCLUSION OF THE ABDOMINAL AORTA

Thrombotic or embolic occlusion of the aorta may produce a dramatic picture Few patients survive and death usually occurs within a few days Cases are recorded however in which patients recovered and records exist in which an old complete occlusion of the abdominal aorta above the bifurcation was an incidental finding at post mortem in some patients only intermittent claudication existed during life while in others no symptoms whatsoever were felt In still other cases the onset of symptoms may be insidious (Leriche syndrome)

According to Shapiro occlusion of the abdominal aorta is found once in 1000 autopsies It appears most often in males between 40 and 60 and rarely in younger subjects The patient complains of fatigue in the legs and pain around the hips and back on walking A systolic murmur may be heard over the abdominal aorta around the umbilicus (Covey) The lower extremities are cold and pale particularly when they are elevated

Femoral pulses and oscillations on the legs are absent Stable erection is impossible Wasting of one or both thighs occurs Thrombosis occurs in atherosclerosis while embolism is most common in rheumatic mitral stenosis Usually

they are combined since an original embolism usually leads to a secondary thrombosis The diagnosis of this condition and its separation from multiple embolism in the arterial tree often is very difficult

It is hard to explain how the collateral circulation is maintained in those patients who develop an occlusion of the lower abdominal aorta without symptoms Embolectomy has been successful in some cases

Patients may survive this syndrome for 10 years but sooner or later gangrene appears

Recently many successful attempts have been made to resect the thrombosed portion of the aorta followed by end to end anastomosis

Syndromes of Gangrene of the Upper Extremities

Dead Fingers

So called dead fingers are not uncommon in otherwise healthy individuals The frequency of this phenomenon in the general population is estimated to be as high as 20 per cent The incidence is equal in both sexes

Often the patient suffered from chilblains in childhood With the onset of puberty (and sometimes in children no more than 8 years old) one or more fingers occasionally exhibit a cadaverous pallor usually beginning at the tip and spreading centrally the episode lasts for only a few minutes Numbness is present and tingling with pain is felt when the circulation returns There is redness due to vasodilatation the consequence of accumulated metabolites with the return of circulation The symptoms are sometimes symmetrical Rarely *the toes are also involved*

Usually the condition is hereditary sometimes it occurs in siblings It appears most often while the person is swimming in cold water Occasionally it develops without exposure to low temperatures but it never occurs for emotional reasons and is never progressive These two factors readily distinguish this phenomenon from Raynaud s syndrome

Rubbing and massage of the finger accelerates the return of the circulation in some cases

The condition is harmless and requires no treatment It may disappear spontaneously *in the course of several years* No nutritional disturbances are visible Hyperexcitability of the peripheral vessels which makes them react abnormally to cooling is considered the releasing cause

Raynaud s Disease and Phenomenon

The Raynaud phenomenon is sometimes found in periarteritis nodosa thromboangitis obliterans (here rarely symmetrical) with cervical ribs in the scalenus anticus syndrome and other conditions discussed in the following pages One speaks of Raynaud s disease when an observation period over several years

reveals no etiology for the condition As opposed to Raynaud s phenomenon Raynaud s disease is usually symmetrical

Raynaud s phenomenon comprises cases of intermittent pallor and cyanosis on exposure to cold This is also a characteristic sign of Raynaud s disease Long after Maurice Raynaud s paper appeared it was shown that all but one of his cases actually belonged to another related group of lesions but his description is so classic that his name should be retained for this syndrome In order to avoid confusion however we will discuss here chiefly the condition which should bear the name Raynaud s disease

In the majority of cases it involves young women although it does occur in men (Hines and Christensen) There is also a hereditary factor Sometimes the patients are neuropathic but otherwise they are usually healthy In many patients the alterations may involve the toes as well

On sudden exposure to cold or on excitement a few or all fingers and sometimes even parts of the hand show a marked purple blue cyanosis or pallor Cyanosis is more common it has been shown that the waxy appearance of the fingers is found only if the blood is massaged out of the part flows out on elevation or is pressed out by reflex spasm Temporary return of the blood flow causes a pink color that quickly turns to blue if the circulation stops again The order of the color change stressed so strongly in the older literature on this subject is of no importance Pain may be excruciating particularly with the return of the normal circulation The involved parts of the extremities often perspire profusely

The excitement that initiates the attack may be a minor one Attacks may appear during ward rounds they may even be caused by a sudden knock on the door (Hunt) An attack may even appear if the patient sits quietly in a room with the temperature of only 18°C The critical temperature initiating an attack varies in different cases

The lesion is often progressive The attacks last longer and occur more often Sometimes the vascular spasm relaxes only after many hours Trophic disturbances develop in such cases There are small areas of necrosis in the skin over the fingers gangrene of large areas does not appear The skin becomes atrophic and there are disturbances of pigmentation The nails show trophic changes and decalcification with atrophy can be demonstrated early in the terminal phalanges by x ray Symmetrical gangrene appears

According to Raynaud the disease is a vasoneurosis resulting from a disturbance of the sympathetic nervous system It has been shown however that attacks also occur after interruption of the sympathetic nerve pathways The essential factor in most cases seems to be an abnormal excitability of the digital arteries to cold Participation of the smaller arterioles and venules in the spasm has not been demonstrated It has also been shown that it is possible to elicit the attacks regularly by exposing the fingers to water at a temperature between 15 and 18°C for 10 to 20 minutes (Lewis) If the hands are exposed to water under 10°C attacks do not occur Attacks appear however when the

body is cooled and the fingers are kept warm warming the body may relieve the attack

While the investigations by Lewis and his co workers make an abnormal reaction of the digital arteries most probable as an etiologic factor it is possible that an abnormal reaction to sympathetic impulses is important although the fact that the attacks may persist after sympathectomy speaks strongly in favor of Lewis conception

In typical Raynaud s disease there is no evidence of occlusion of larger arteries In more advanced stages intimal thickening of the digital arteries appears with secondary occlusion of small vessels partly by thrombosis and makes the appearance of nutritional disturbances and gangrene understandable With the narrowing of the lumen in these arteries even a slight increase in vascular tone on exposure to cold may interrupt the blood flow (Lewis)

With regard to therapy patients are advised to keep the hands warm and to avoid exposing other parts of the body to cooler temperature If possible the patients should move to a milder climate

Temporary improvement has been reported with ACTH and cortisone Priscoline (25—50 mg three times a day) and Roniacol help some patients

Cervical sympathectomy affords good results Even if the attacks recur after some time or remain they are milder shorter and less frequent Operations are inadvisable in very advanced stages when arterial obstruction is present The beneficial effect of neurosurgery proves that nervous factors play some part in the attacks The gradual reappearance of pain after the operation may be due to an increased sensitivity of the vessels to adrenalin following sympathectomy

Preganglionic operations are preferable in the upper extremities The rami of the second and third thoracic ganglia are divided In the lower extremities extirpation of the second and third lumbar ganglia is necessary Special care must be taken to avoid regeneration

Dermatomyositis may cause heliotrope color of the skin pigmentation asthenia and the Raynaud phenomenon It is occasionally associated with visceral disease which may precede the dermatomyositis Recovery may occur but usually the illness is fatal

In addition to the other syndromes leading to the appearance of *Raynaud s* phenomenon those due to the presence of cold agglutinins (Hausen) and cold precipitable proteins (cryoglobulinemia) occasionally encountered in myeloma should be mentioned (Barr et al)

Scleroderma

This is in many respects a mysterious disease of unknown etiology and one not susceptible to successful therapy Since it is often seen in patients with Raynaud s phenomenon it may be briefly discussed at this place

Although a differentiation is made between generalized scleroderma and the localized form (sclerodactyly acrosclerosis) it is not always possible to separate these conditions for one may merge into the other

The condition may start without vasomotor disturbances in *other cases* it begins after a typical Raynaud s syndrome For the most part it affects young *females* the ratio of incidence in the two sexes is 10 to 1 (Hunt)

The hands feet and face are usually involved the trunk is rarely affected *The* skin becomes shiny the normal wrinkles disappear and it is impossible to *fold the* skin at the finger tips Flexion and extension of the fingers become difficult the hair disappears the nails grow slowly and show trophic disturbances Sores and blisters appear at the tips of the tapering fingers

If the face is involved the masklike facies becomes devoid of expression The creases disappear and the mouth cannot be opened normally the eyes cannot be closed in advanced cases Disturbances of pigmentation appear Histologically there is hypertrophy of the collagen tissue which causes constriction of the blood vessels (Matsui)

With greater involvement of the skin there is considerable vascular constriction but the disturbed nutrition of the skin is not the primary causative factor since the condition often occurs without vascular disturbances moreover nutritional disturbances of other origin than Raynaud s fail to cause scleroderma

Perhaps the lesion is of toxic origin the possibility of an endocrine influence has been discussed Posterior pituitary extracts have been administered Often the process progresses very fast from the start and the prognosis is poor Patients become crippled since they are unable to move the fingers However patients may live with this illness in a tolerable condition over three decades

Myocardial fibrosis and dysphagia with esophageal strictures indicate that the process may be generalized in some cases The lungs kidneys adrenals pancreas larynx and tongue may also become involved although this is rare When affected these parts show fibroblastic proliferation

The disease may progress slowly Treatment is purely symptomatic Massage of the skin with olive oil brings some improvement Iontophoresis with mecholyl and histamine has been recommended Ganglionectomy is done and affords slight relief in cases in which a vasospastic component can be proved Other observers have obtained no success from the operation

Therapy with ACTH and cortisone causes temporary improvement Exacerbations during therapy with corticotropin have been noted (Lunseth et al) Treatment with veratrum alkaloids (1—3 mg of Veriloid three times daily) has been recommended (Fuller) Spontaneous remissions occur Patients often die from heart failure

Often *scleredema* is confused with scleroderma In the former the hands are not involved the skin is not atrophic and there is no depigmentation It is a benign self limited edema of the face arms and legs pleural and pericardial effusions occur

Acrosclerosis is separated from diffuse scleroderma only with difficulty There is swelling of the collagen fibers of the skin absorption of the terminal phalanges in the x ray and cutaneous ulcers and gangrene

Cervical Rib and Scalenus Anticus Syndrome Hyperabduction and Costoclavicular Syndrome

The occurrence of a cervical rib was known to Galen but disturbances caused by this abnormality have been recognized only in the last 70 years

Cervical rib is not a rare abnormality It may occur bilaterally The brachial plexus and the subclavian artery travel over the cervical rib laterally and downward

Cervical rib is more common in women than in men (Adson and Coffey) The first symptoms begin late (between the age of 25 and 50) presumably due to the fact that with advancing age the shoulder sags lower leading more readily to compression of the structures named above In right handed persons the right side is much more often involved than the left

The symptoms consist of burning pain sometimes of lancinating character felt mostly in the ulnar side of the arm and over the deltoid area Numbness tingling and some hyperesthesia appear The fingers and hand may be cold and discolored A bluish hue or redness appears in some cases while pallor is present in others There is abnormal perspiration and some swelling Muscular weakness may be followed by trophic changes and even gangrene The area of attachment of the scalenus muscle is often tender The blood pressure on the involved side may be lower

Sometimes x ray examination shows the presence of a cervical rib Lifting the shoulder may furnish temporary relief (Falconer and Weddell) whereas sudden rotation of the head or downward movement of the shoulder may cause pain

Opinions concerning the mechanism of the disturbances vary The original explanation which is still accepted by most authorities attributes the lesion merely to compression of the subclavian artery According to Lewis and Pickering damage of the endothelium leads to the formation of local thrombosis in the subclavian artery Migration of these thrombi to the periphery causes ulcers and gangrene of the fingers At post mortem one may actually find the subclavian artery imprisoned in dense bands (Oljenick) It is believed by some that irritation of the nerves also produces symptoms and signs Since the lancinating pain cannot be explained by a disturbed arterial blood supply irritation of the sympathetic nerves in the brachial plexus was considered a factor irritation with resultant vascular spasm was advanced as the cause of the syndrome (Telford and Stopford) The presence of excessive perspiration in the involved area speaks in favor of the latter conception In all probability a combination of these factors is significant

Surgical intervention is indicated if there is evidence that the complaints are progressive Resection of the cervical rib (if present) has been replaced by tenotomy of the scalenus anterior muscle at its attachment on the first or cervical rib (Adson and Coffey) The operation is usually but not invariably successful

Even in the absence of a cervical rib similar peripheral vascular phenomena may appear due to the fact that the subclavian vessels and the brachial plexus are situated in the angle formed by the attachment of the scalenus anterior muscle and the first rib the muscle or fibrotic bands may compress the artery and nerves under certain conditions (scalenus anticus syndrome) The deepest structure in the angle is the subclavian artery above it follow the eighth cervical and first dorsal nerves If a cervical rib is present the scalenus muscle inserts on it

In some cases particularly during deep inspiration the subclavian artery may be compressed between the clavicle and the ribs One type of paradoxical pulse results from this compression and in one personally observed patient a systolic murmur was heard over the subclavian artery in inspiration due to compression Hyperabduction of the arm for a long period e g sleeping on the hyperabducted arm may also compress the subclavian artery between the clavicle and first rib and seriously diminish the blood supply to the arm Pressure by crutches may cause a similar syndrome

Some Other Types of Gangrene

Syndromes associated with disturbed blood supply to the arms and productive of gangrene are observed in several other conditions that are often confused with the Raynaud syndrome

Ball Thrombus in the Left Atrium This condition is found exclusively in rheumatic mitral stenosis and causes a rather typical clinical picture with cyanosis and gangrene of the fingers toes the tip of the nose and ear It should be easily diagnosed and was discussed before

Infections Peripheral gangrene occurs following certain infections e g syphilis typhus meningococcus infection and infrequently in rheumatic fever

Intoxications Ergot and phenol may cause peripheral gangrene In some patients gangrene of fingers and toes has followed the injection of one ml of a standard ergot preparation used in the treatment of migraine or in obstetrics If the evaporation of phenol is prevented by a bandage local gangrene may follow

Symmetrical Gangrene of the Young Symmetrical Gangrene of the Old Rarely these conditions develop within a few days without apparent cause In the former an infection often precedes atherosclerosis or tuberculosis may be responsible in the latter But in young and in old patients symmetrical gangrene may develop in the absence of any other evidence of disease and particularly without signs of an infection or intoxication

In a 65 year old man of this group observed by one of us dry symmetrical gangrene developed on all fingertips within a few days There was no pain and no other evidence of disease

Hemoglobinuria Occasionally cold hemoglobinuria may cause symmetrical gangrene These patients usually have syphilis and may develop gangrene

after exposure to cold Damage of the vascular endothelium leads to arterial thrombosis

Diseases of the Central Nervous System In some diseases particularly in anterior poliomyelitis hemiplegia and syringomyelia disturbances of the circulation without gangrene are occasionally observed The peripheral circulation is abnormal if the limb is not used and muscles are inactive

Diseases Caused by Vibrating Tools Workers using vibrating tools pneumatic hammers pounding machines in shoe factories chisels and riveting machines may present a disturbance similar to Raynaud s syndrome These patients show evidence of a disturbed blood supply in the fingers and hands they are sensitive to cold and so forth The syndrome disappears quickly if the workers change their occupation when the first symptoms of the Raynaud phenomenon start But once established the condition usually persists even if the patient no longer uses such tools (Jepson) The pathophysiology is unknown The endothelium is not involved and therefore serious nutritional lesions are missing

Other Factors It may be mentioned again that in thromboangiitis obliterans as well as in peripheral atherosclerosis a Raynaud like syndrome is occasionally observed

Finally symmetrical gangrene has been seen in simple cardiac failure and has been explained by a reflex vasoconstriction (Perry and Davie)

ACROCYANOSIS

This condition formerly called a vasoneurosis appears almost exclusively in young women Whether an endocrine imbalance is responsible is unknown

The fingers and rarely the toes as well exhibit a marked cyanosis They feel cold and swollen particularly during the winter The patients also complain of excessive perspiration Fissures occur in the skin over the fingertips and the nails are altered Chilblains are common Pain is absent Cold aggravates the complaints and excessive warmth is also poorly tolerated In warm temperatures as well as when it is excessively cold the fingers are somewhat purple in color

In some instances the condition is purely symptomatic It occurs for example in thromboangiitis obliterans or after refrigeration

The mechanism is unknown Originally explained as an obstruction of venous drainage (Erben) it was believed later (Lewis and Landis) that the essential disturbance consists in an abnormal narrowing of the arterioles with widening of the capillaries and veins this diminishes the blood supply and causes oxygen deficiency in the vessels of the subpapillary plexus There is no vasomotor disturbance but only a local abnormal response in the arterioles Others assume that dilatation and lack of response in the capillaries and venules of the skin slows blood flow

The therapy is simple and consists merely in advising the patient to keep the hands warm

LIVEDO RETICULARIS

This condition characterized by mottled skin with focal bluish discolorations is recognized lately as a vascular disease It occurs mostly in women and involves the legs and feet Exacerbations occur in the summer months According to Feldaker et al 30 per cent of the patients have hypertension 50 per cent have emotional instability Particularly in cold weather numbness and pain appear vasospasm may be responsible but arterial occlusions are found Ulcerations of the skin gangrene and loss of the toes and limbs are reported Ganglion blocking agents (hexamethonium) and sympathectomy are recommended

ERYTHROMELALGIA

This condition was originally described by Mitchell in 1878 Believed to be a rare vascular disease it is currently assumed to be a syndrome common to several conditions and not an entity in itself (Lewis)

There is a unilateral (rarely bilateral) painful red swelling limited to a part of the extremity usually the leg The essential features are burning pain increased local heat increased pain on warming the involved area and on dependency improvement on cooling elevation and rest (Brown) The local heat has been explained by a dilatation of the arterioles the redness by a dilatation of capillaries and venules

According to Sir Thomas Lewis the condition is the result of an abnormal response of the arteries to warmth The skin is highly susceptible and sensitive to friction as well as to temperatures over 32°C The disturbance depends upon the liberation of a specific substance (histamine?) The name Erythralgia has been proposed (Lewis) Smith and Allen refer to it as Erythermalgia

A similar condition occurs after burns of the skin and is observed occasionally in polycythemia It is not rare in thromboangiitis obliterans

The therapy consists in keeping the involved area cool Good response has been observed after administration of epinephrine (Mufson) and the relief experienced after taking acetylsalicylic acid has been called specific (Smith and Allen) The condition may improve following sympathectomy

CAUSALGIA (REFLEX SYMPATHETIC DYSTROPHY) AND POST TRAUMATIC DISTURBANCES

Very painful circulatory disturbances are known to occur occasionally after trauma to a limb Mitchell called this condition causalgia owing to the burning character of the pain

Originally it was thought that the lesion was due to post traumatic spasm of the injured artery Vascular spasm from mechanical irritation is known to every physician The spastic vein which scarcely permits the introduction of a canula and the spastic artery met with in experiments on animals are well known to medical students Prolonged arterial spasm lasting for hours has been observed

following blunt trauma It was gradually recognized however that vasodilatation and not spasm is responsible for many of the symptoms and signs of causalgia and that nerve irritation alone without any trauma to an artery may be the essential factor

Prolonged bombardment of the spinal cord with pain impulses sets up a circle of reflexes similar to the painful disability of the shoulder in coronary disease These impulses spread via the connecting neurons of the internuncial pool up and down and across the spinal cord and set up disturbances in other segments The name reflex sympathetic dystrophy has been proposed since pain may be slight or missing

There is no parallelism between the severity of the condition and the degree of trauma The causalgic state may follow rather trivial trauma and it is estimated that some evidence of it occurs in about 5 per cent of cases after sprains The syndrome may begin hours after the trauma Because the original injury may be slight patients are treated as neurotics

The first sign is pain out of proportion to the injury The pain is continuous but it may also be intensified in paroxysms which last for hours In this stage there are no objective findings and the diagnosis of a compensation neurosis or malingering is often made Redness soon appears in the skin over the involved area and there is tenderness to touch and to friction The skin feels warm and later cold there is marked perspiration at this time The situation is similar to that found in erythromelalgia The pain may increase until it is excruciating and intractable Even chordotomy has been performed without benefit in these cases and it has been even suggested that the sensory cortical centers be removed

Presumably due to the vasodilatation and increased blood flow bone atrophy (Sudeck s atrophy) sets in (Leriche and Fontaine) the skin may be edematous and the muscles atrophic largely as the result of disuse

With respect to treatment everything must be done at the beginning of the syndrome to relieve the pain infiltration of the injured area with procaine has proved useful in more advanced stages paravertebral sympathetic block is recommended or finally preganglionic sympathectomy

Priscoline may be given in doses of 25—50 mg four or five times daily Cortisone and ACTH have been employed with some success Recently ganglion blocking agents (hexamethonium and dibenzyline) have been used with success (Fowler and Moser)

THE PULSELESS DISEASE

Definition The pulseless disease — maladie sans pouls or Takayashu s syndrome — concerns a clinical picture described more than a century ago in single observations It became a recognizable and well defined syndrome after Takayashu s description

Pathology Etiology Syphilis is a factor in some cases since syphilitic aortitis obstructs the orifices of the large vessels originating from the arch of the

aorta In most patients an angiitis has been found with intimal proliferation (Mangold and Roth) It has been called an angiitis obliterans Others discuss the possibility of a dysontogenesis (Trias de Bes et al) It is possible that the etiology varies from patient to patient

Symptoms Usually young women are affected although it has been observed in both sexes after the age of 50 The patients complain of headaches particularly if the head is moved backward There are attacks of fainting vertigo and loss of consciousness if the patient changes her position quickly The heaviness and pains in the arms on working may resemble intermittent claudication There is also an intermittent claudication of the muscles used in mastication Very often there is dimness of vision photophobia amblyopia and transient amaurosis cataract visual disturbances of various types up to complete blindness which may bring the patient originally to the ophthalmologist Coronary artery involvement is rare

Signs The most outstanding clinical sign is the absence of the pulse of the arteries of the aortic arch i e in one or both carotids left and right subclavian Sometimes in one artery or another a small pulse is present but it soon disappears Trophic disturbances have been described in the skin muscle and even the skeleton in areas with an abnormal blood supply An ulcerated nose and palate occur The blood pressure in the lower extremities is often increased Therefore and because of the presence of a collateral circulation involving deeper arteries (affecting the same vessels as in coarctation of the aorta only with a reversed direction of blood flow) one often speaks of the syndrome as an inverted coarctation Even crenation of the lower border of the ribs due to enlarged tortuous intercostal arteries has been described (Ask Upmark) A systolic diastolic machinery murmur can be heard in the supraclavicular area near the attachment of the sternocleidomastoid muscle due to the widened collaterals with great speed of blood flow

There are many findings when the eyes are examined Corneal opacities atrophy of the retina iris pallor of the fundus low pressure in the retinal vessel glaucoma and cataracts in particular appear

Course There is occasionally an acute form which soon causes death Often the disease progresses insidiously for a few years the longest known case lived 14 years (Ask Upmark) The prognosis is poor

Therapy is unknown Favorable experience with cortisone and ACTH remains to be secured

PERIARTERITIS NODOSA

Although periarteritis nodosa is an uncommon disorder it is by no means as rare as was formerly believed At the last count well over 1000 cases had been reported since the original observations of Kussmaul and Maier in 1866 With the publication of series rather than individual cases the number is rapidly mounting

There is increasing evidence to indicate that periarteritis nodosa is not a disease sui generis. With this convenient term several types of necrotizing pan arteritis are designated. The uncertain nosologic status is reflected in the existence of approximately 20 synonyms of which periarteritis nodosa and polyarteritis nodosa are most commonly used with a gradual shift toward the latter.

Etiology

The cause of the disorder is unknown. Syphilis is not an etiologic factor although many of the early cases occurred in luetic individuals and the Wassermann reaction is occasionally positive. A filterable virus has been considered responsible in order to account for the epidemic appearance of periarteritis nodosa in lower animals but no supporting evidence has been obtained.

The disorder is likely to occur in individuals who have suffered from asthma, serum sickness, various infections, sulfonamide reactions and the like and it seems probable that a hyperergic reaction is responsible. This suggestion finds experimental support in the production of the characteristic lesion in rabbits by repeated injections of horse serum. The relation to the changes found in rheumatic fever has been stressed repeatedly.

Under certain conditions an infectious or chemical agent may alter the response of the vascular wall so that it reacts abnormally to a variety of stimuli (allergic hyperergic response).

Periarteritis nodosa occurs at all ages but it is most common between the ages of 30 and 40. Nearly 70 per cent of those affected are males (Boyd).

Pathology

The arteries affected belong primarily to the muscular type and the size of the vessels involved ordinarily does not exceed that of the hepatic artery. The location of the lesion in a given vessel depends on the size of the artery and the presence of vasa vasorum. In the larger arteries changes are prominent at the junction of the media and the adventitia but in small vessels the lesion may remain for the most part subintimal. It is the tendency of the process to involve the medio adventitial junction that led to the name periarteritis, while the fact that destruction of the elastica was often followed by aneurysmal outpouchings suggested the term nodosa. Moreover the lesion is discontinuous and affects only limited sections of an artery.

The initial necrosis is followed by leukocytic infiltration, exudation and the development of granulation tissue. The elastic membranes are particularly susceptible and may be destroyed. If the inflammation extends through all layers of the vessel the elastic layers are destroyed and the media is necrotic. Small aneurysmal nodules, firm pinkish or red and varying in size from one to several millimeters, may be scattered irregularly along the affected artery. If the artery ruptures — a rather common event in the renal and perirenal structures — massive hemorrhage may result. In smaller vessels the major lesion may be subintimal

in this case local thrombosis may result in occlusion of the vessel and an infarction of the tissues supplied by the artery an event not unusual in the mesenteric arteries and the intestine Irrespective of the location of the lesion in the adventitial or subintimal area the exudate is often composed largely of eosinophiles a fact which lends further support to the possibility of allergy as an important etiologic factor

There is a subacute phase with evidence of repair so that intimal proliferation may be found adjacent to medial necrosis Moreover a chronic state is seen in which the inflammatory processes have vanished in this instance the lumen of the vessel has usually been closed owing to proliferation of the intima and thrombosis while the media may show calcium deposits Since the affection is often characterized by exacerbations and remissions all kinds of lesions from fresh to healed may be observed at necropsy

Although the involvement of the veins is less common and much less conspicuous in occasional cases the participation of the venous system is prominent with the result that clinical as well as histologic similarities between periarteritis nodosa and thromboangiitis obliterans exist

Symptoms and Signs

The clinical picture is remarkably diversified since arteries in practically every region of the body may be affected in varying degrees either simultaneously, in sequence or individually Moreover the process acts with variable intensity on different arteries and even on a single artery thus mild involvement of a mesenteric artery may slightly interfere with the blood supply of a portion of the intestine and cause intermittent colicky pain Furthermore the intestine may be infarcted and fatal peritonitis develops with fulminating speed

Even the onset varies from insidious to violent Often a tonsillitis or some other infection precedes the illness by a few weeks or months Sometimes after the patient seems to have recovered from the preliminary illness a new syndrome either in a new guise or simulating the old illness gradually emerges There may be loss of weight leukocytosis and increased sedimentation rate

In the ordinary case the impression created at the onset is that of a subacute febrile disease without particular localization Typhoid fever miliary tuberculosis or subacute bacterial endocarditis are usually suspected but no confirmatory evidence of these diseases can be obtained The situation is equally confusing if the affection does seem to localize If there are pains in the muscles with eosinophilia and fever trichinosis may seem likely and leads to muscle biopsy if the pains recur in the joints and an erythema develops with obscure fever rheumatic fever may be simulated Not rarely the abdominal symptoms dominate the clinical picture the fever abdominal pain the leukocytosis and evidence of peritoneal irritation suggest an acute cholecystitis or appendicitis necessitating operative intervention Not only does the surgeon fail to recognize the situation but the pathologist may overlook the lesion in the specimen and to his embarrassment discover the typical process when the material is reviewed at the necropsy

In rare instances the surgeon has noted the presence of aneurysms of the hepatic or other abdominal arteries

The fever does not follow any special course it may be high low or absent Prolonged remissions may recur between febrile episodes We have repeatedly encountered an irregular temperature closely simulating Pel Ebstein fever of Hodgkin s disease

Since the manifestations are protean reference will be made only to some of the clinical prototypes and outstanding phenomena in the succeeding paragraphs

Skin In rare cases the affection seems limited to the cutaneous vessels This rather prolonged and relatively benign type is recognized with the appearance of livedo racemosa and nodules The livedo consists of a flash of lightning discoloration in which the vessels are thick elevated blue red and dendritic *In the meshes of the livedo* eruptions of various types occur Livedo racemosa may also occur in other diseases (see above) and must be associated with the nodules to be diagnostic

The nodules are isolated subcutaneous shiny round pinhead in size move able and painful At times the nodules are somewhat larger and may attain the size of a pea in the subcutaneous form These nodules may break down and form ulcers Recovery usually occurs in this form although it may be postponed for two or three years

Subcutaneous nodules occur in about 20 per cent of cases of periarteritis nodosa when the abnormal findings consist for the most part of these nodules the term periarteritis nodosa subcutanea is sometimes applied The nodules tend to appear in crops on various parts of the body although the extensor surfaces are the most common site The number of nodules present at a single time usually *does not exceed 50 The appearance of a crop of nodules often coincides with* a new bout of fever

Ordinarily the nodules disappear in the course of a few weeks if no ulcer develops If numerous or large arteries are involved cutaneous apoplexy may follow or multiple areas of gangrene may occur and even simulate Raynaud s disease (Freund)

With or without subcutaneous nodules crops of petechiae may be found Although a variety of erythematous eruptions may be encountered purpura of the Schoenlein Henoch type is the most common

Owing to the secondary anemia which often develops pallor may be pro *nounced This is* common and with the wasting observed in some patients led to the old name chlorotic marasmus Apart from the pigmentation following subcutaneous hemorrhages a discoloration of the skin resembling that of Addison s disease is occasionally seen

Muscles and Nerves The neuromyositic manifestations are very important and may be explained by the involvement of the vessels supplying muscles and nerves Polymyositis (Fahr) is extremely common and often the correct diagnosis is established when a muscle biopsy is secured for suspected trichinosis Any or all of the skeletal muscles may be affected It is common to consider the possibility

of a dermatomyositis when the cutaneous and muscle symptoms are prominent sometimes differential diagnosis is impossible

In addition to a polymyositis there is often a polyneuritis characterized by pain weakness nerve trunk tenderness disturbance of sensation atrophy and paralysis A peroneal forearm type is rather common If an acute febrile polymyositis and polyneuritis is accompanied by albuminuria periarteritis nodosa should be suspected

In a minority of patients occlusion of the deep muscle arteries occurs or the peripheral vessels of an extremity become occluded and the segment supplied becomes gangrenous In this form designated periarteritis nodosa mutilans the clinical picture may approximate that of thromboangiitis obliterans

Abdomen The arteries supplying any abdominal organ may be involved thus producing a variegated clinical picture Involvement of the mesenteric arteries may be responsible for colic alterations of the bowel habit intestinal infarction or peritonitis Sometimes symptoms typical of an appendicitis may antedate all other symptoms for several months In one personally observed case polyneuritis and polymyositis developed four months after the patient had recovered from an appendectomy her eosinophilia did not recede in the interim The vessels of the gall bladder are frequently involved so that operations are undertaken for cholecystitis Gastric ulcers are not infrequent and hemorrhage is not unusual Pancreatic involvement is not ordinarily detected by clinical methods but diabetes mellitus has developed in rare cases periarteritis nodosa is one of the few causes for infarction of the pancreas

Despite these and innumerable other possibilities the most common abdominal symptom in periarteritis nodosa is vague pain usually epigastric or shifting from left to right in the course of a subacute or prolonged febrile illness The diagnosis of periarteritis nodosa is suggested in these cases by the finding of a polyneuritis polymyositis albuminuria and eosinophilia At any moment an abdominal organ may be infarcted causing hemorrhage or peritonitis to develop

Kidneys Sooner or later in the course of most cases (80 per cent in our experience) the kidneys are affected The urine contains albumin casts and other evidence of a tubuloglomerular nephritis It is however the rapid development of hypertension in the course of a febrile disease that makes periarteritis nodosa a diagnostic possibility While the elevation of blood pressure is not limited to febrile patients its sudden appearance and rapid evolution in nearly 50 per cent of the patients makes it an important sign Rather often the urinary signs the edema of the extremities and the hypertension lead to the diagnosis of an acute nephritis naturally the differential diagnosis between nephritis and periarteritis nodosa may be impossible if the vascular lesion is limited to the kidney

In a small number of cases the outstanding symptom is hematuria Instances are known in which essential hematuria led to nephrectomy for severe and recurrent bleeding and periarteritis nodosa was discovered in the specimen removed This form in contrast to the type simulating nephritis has a relatively benign course

More catastrophic is a variety in which periarteritis nodosa affects the kidney vessels. Rupture of these *interlobular arteries may be followed by perirenal* hematoma and collapse. Hemorrhage is common in all forms of periarteritis nodosa and accounts for many instances of shock seen in this disease. The diagnosis usually is not considered unless a mass suddenly develops in one or the other flank.

Renal infarction is also very common and terminal uremia is the usual outcome of those patients not succumbing to a vascular accident.

Heart. Tachycardia out of proportion to the fever is often observed and militates against the diagnosis of typhoid fever. In spite of the involvement of the coronary arteries, angina pectoris is rather uncommon. Sometimes the aneurysms of the coronary arteries in this disease resemble the "beads of a rosary," but some of the cases of multiple coronary artery aneurysm reported in very young children undoubtedly belong to the congenital miliary aneurysms resulting from malformations of the arteries, rather than to periarteritis nodosa.

When there is an irregular fever and cardiac murmurs develop as the result of cardiac dilatation and anemia, the suspicion of a subacute bacterial endocarditis is almost inevitable. This suspicion may be strengthened by the development of infarctions, hematuria, petechiae and the like. The electrocardiogram may show evidence of myocardial damage but is not altered in any characteristic manner. Myocardial infarction is uncommon despite the occurrence of multiple aneurysms of the coronary arteries. Involvement of the pericardial vessels may cause an inexplicable pericarditis.

Congestive heart failure often supervenes and is, next to uremia, the most common ending of fatal periarteritis nodosa.

Lungs. In a large number of instances the syndrome of periarteritis nodosa seems to emerge from a previous history of bronchial asthma. Not infrequently there is definite evidence of an allergy, and the development of an increasingly severe, intractable bronchial asthma after some mild illness should raise the question of the possible presence of periarteritis nodosa. It has been suggested that the diagnosis of periarteritis nodosa should be considered in cases of bronchial asthma with more than 15 per cent eosinophiles (Wilson and Alexander).

In many cases the persistent low grade fever together with indefinite chest signs make the diagnosis of pulmonary tuberculosis likely. While x-ray changes may occur in the lungs of patients with periarteritis nodosa, they are not characteristic nor do they simulate those of tuberculosis. The occurrence of pulmonary infarction and pulmonary inflammation may cause marked dyspnea and cyanosis during the course of the illness.

Endocrine Glands. The endocrine glands have not been thoroughly studied in periarteritis nodosa but case reports are sufficient to show that they may be involved. Apart from the better known involvement of the pituitary (syndromes like Simmond's cachexia) and the adrenals (syndromes resembling Addison's disease), no special clinical prototypes have been described.

Central Nervous System. Symptoms and signs arising in the central nervous system are observed in a minority of cases. As might be anticipated they are

subject to great variation Occasionally in a patient with periarteritis nodosa meningitis was diagnosed until a negative spinal fluid was obtained Epileptiform attacks occur Likewise a variety of neuropsychiatric syndromes have been reported in older patients suffering from periarteritis nodosa but none of them are characteristic

Eyes Albuminuric retinitis is exceedingly common detachment of the retina is occasionally observed and total loss of vision has been recorded Aneurysmal dilatation of small fundal vessels has been seen Any of the intrinsic or extrinsic muscles of the eye may become paralyzed

Laboratory Findings

Laboratory findings are sometimes of diagnostic help The secondary anemia of moderate intensity gives little assistance As a rule the white blood cell count ranges between 12 000 and 20 000 In contrast to typhoid fever leukopenia is exceptional The increase in the number of white blood cells is due to a polymorphonucleosis but the percentage of polymorphonuclear cells does not rise to that ordinarily seen in miliary tuberculosis At least 10 per cent of the patients suffering from periarteritis nodosa have a marked eosinophilia there are few diseases in which the percentage of eosinophiles may become so high In one personally observed case they reached 60 per cent of the white blood cells while even figures as high as 90 per cent have been reported

Differential Diagnosis

Many of the differential diagnostic problems have been mentioned in the preceding paragraphs Miliary tuberculosis typhoid fever trichinosis neuritis meningitis encephalitis cholecystitis angina pectoris appendicitis bronchial asthma myositis and sepsis are often diagnosed before the true nature of the disease is recognized The diagnosis is inferential until established by histologic sections obtained by biopsy or during the course of some surgical procedure Obscure fever weakness pallor polyneuritis polymyositis vague gastrointestinal disturbances signs of nephritis or hypertension subcutaneous nodules and eosinophilia constitute some of the suggestive symptoms and signs

Allergy hypersensitivity angiitis and serum sickness angiitis must be considered Loeffler s syndrome and temporal arteritis are related In allergic granulomatosis which is related to Loeffler s syndrome granulomatous nodules occur in the epicardium and mural endocardium Clinically fever asthma and signs of vascular disease appear in various organs (Churg and Strauss)

Prognosis

Since most reports have been published by pathologists and major emphasis has been placed upon the tissue alterations attention has been focused on the lethal nature of the affection However the reparative process is often clearly

evident and recovery presumably occurs more frequently than was formerly appreciated

In most cases the duration of life after the appearance of major symptoms is about four months In the event of some catastrophe e g intestinal perforation the clinical course may be measured in terms of days otherwise survival for one or two years is possible when vital organs happen to escape serious damage although this is a rather uncommon occurrence However we observed several cases in medical officers of the last war where the diagnosis had been unequivocally established by classical peripheral symptoms high eosinophilia and positive muscle biopsy in which recovery was more or less complete save for an extreme atherosclerosis of the vessels of the lower extremities The course of the cutaneous forms is often prolonged and recovery with more or less invalidism is not extremely rare The most common causes of death are nephritis cardiac failure perirenal hemorrhages bronchopneumonia or peritonitis

Treatment

Attempts to ascertain the action and exclusion of possible antigenic substances do not seem to have been undertaken With the greatly reduced use of the sulfonamides the incidence of the disease seems to be less A host of measures with a positive therapeutic effect has been suggested which by their very multiplicity implies that none of them has much actual value moreover practically none of the supposedly remedial agents seems very rational if the current theories of pathogenesis are correct Thus the arsphenamines were advocated although the lesion frequently developed during treatment with arsenicals The same holds for the sulfonamides which have also been employed for the experimental production of the lesion Generally speaking agents have seemed to be most beneficial when evidence of visceral involvement was slight that is in the forms known to be associated with spontaneous remission

Therapy in our experience is mainly supportive and symptomatic Blood transfusions may occasionally make the condition more tolerable Special diets a high vitamin diet for example have been advocated but in practice the presence or absence of intestinal or renal involvement will determine the nature of the food permissible

In recent years ACTH cortisone and related substances seem to provide marked improvements Cortisone (?00 mg on the first day and 200 mg daily for 5—6 weeks) or 100—150 mg of ACTH are at present the medicinal agents of choice Often the fever disappears after a few days of such therapy but relapses are common

TEMPORAL ARTERITIS

This disease of unknown etiology was described in 1934 (Horton et al) It affects *patients over 50 years* of age most are between 70 and 80 although one patient was only 23 years old Women are more often affected than men

It begins with malaise vomiting pain in the ears and in the temporal area of the affected side and fever up to 39 5 C There is anorexia severe nocturnal headache and weakness After a few weeks there is a definite periarteritis around the temporal artery although the vessel still pulsates Soon it becomes thrombosed and very sensitive to the touch The palpable nodules consist of the thrombosed vessel and the periarterial inflammatory tissue Mastication becomes very painful Leukocytosis appears

In rare cases other arteries are also involved One even speaks of a cranial arteritis in those instances in which these arteries but not the temporal artery are affected Ocular complications seem to occur in one third of the patients owing to involvement of the ophthalmic and retinal arteries Blindness and visual disturbances are possible consequences In one case of bilateral temporal arteritis total blindness appeared (Shannon and Solomon) Apparently the visual disturbances are permanent

The disease is self limited After four to twelve months the symptoms and signs gradually subside or at least fail to progress an occasional case with a more protracted course is encountered

The histologic picture is similar to that seen in periarteritis nodosa The lumen of the artery is filled by granulomatous tissue with giant cells At present nothing is known about the histologic findings in other arteries of the body

Treatment is mainly symptomatic Potassium iodide has been recommended and ACTH and cortisone induce temporary remissions

Dramatic improvement may appear if the involved segment of the temporal artery is removed even infiltration with novocaine aids temporarily

ARTERIOVENOUS ANASTOMOSES AND GLOMUS TUMOR

Congenital and acquired arteriovenous fistulas were discussed in a previous chapter At this juncture reference will be made to some peculiar short circuits between arteries and veins which were described in classic papers many years ago but failed to attract much attention from physiologists and clinicians until their part in pathology was discovered by Masson in 1924

The Normal Glomus

Anatomy Some of the digital arteries divide into two branches One takes the normal course and divides into arterioles and capillaries which transport the blood finally into the veins while another branch sends blood directly from the arterial side into a vein The anastomotic vessel the Sucquet Hoyer canal has a very thick wall and is slightly tortuous It has a longitudinal and circular layer of muscle The outer muscles may be completely replaced by epitheloid cells This vessel suddenly changes its character and joins wide veins to form a convolution covering and surrounding the anastomotic artery The veins have no muscular fibers and only a thin layer of endothelium There are many collagen fibers between

these vessels and many nonmedullated nerve fibers A capsule consisting of connective tissue surrounds the whole structure Such a unit was called a glomus by Masson after the glomus coccygeum which has a similar structure Sometimes four Sucquet Hoyer canals originate from a single anastomotic artery

The glomus is situated in the deepest layer of the corium particularly on the fingers the nail beds the toes hands the foot The number of these structures has been estimated to be up to 500 per square centimeter (Grant and Bland) but is certainly less

According to most investigators the glomus appears in the first year after birth but it has been found in an embryo of six months (Clara) Their number diminishes in old age (Popoff) They are not found in cold blooded animals

Physiology Our knowledge of their function is limited It is certain that an anastomotic artery can close or open if the need arises that is the blood can be directed in the normal way through the capillaries or it can be shunted into the glomi Therefore Hoyer thought that these structures might play a part in the regulation of temperature Experimental observations have been made which favor this conception (Grant and Bland Lewis and Pickering) When cold is applied to the skin the anastomosis opens and warm arterial blood flows into the venous convolution Whether the glomus plays any part in the regulation of blood pressure is not decided

The appearance of arterialized blood in the arm veins in the tropics observed early by Robert Mayer the appearance of arterialized blood in the submaxillary vein during stimulation of the chorda tympani seen by Claude Bernard and other observations in kidney experiments are explained by these short circuits and *support the assumption that such anastomoses occur also in other organs* Arterio venous short circuits were observed in the scleral conjunctiva (Urbanek and Scherf)

In this connection it is of interest that epitheloid cells similar to those found in the glomus are seen in the wall of the afferent arteries of the glomeruli of the kidney

THE GLOMUS UNDER ABNORMAL CONDITIONS

The behavior of the glomus in peripheral vascular diseases has been studied (Popoff) Changes have been seen in peripheral atherosclerosis where the afferent arteries are sometimes found continuously patent This may explain why the affected extremity often is warmer than the normal one Fewer changes are found in thromboangiitis obliterans but *certain symptoms and signs of this condition* have been ascribed to an abnormal function of the glomus

It is a very interesting fact that the blood of the saphenous vein in patients with atherosclerosis of the leg arteries often is more arterialized than the blood of the basilic vein (Popoff) This finding has been frequently confirmed it may be due to the patency of afferent arteries of the glomus

Glomus Tumor

Small painful subcutaneous tubercles were described early but since Masson's study their relation to the glomus (glomus tumors) and their common occurrence has become more widely appreciated

These glomus tumors are small bluish nodules of firm consistency and exquisite sensitivity to touch Usually they are found at the same areas as normal glomus formations They appear most often on the fingers particularly in the nail bed but are occasionally seen in areas where the glomus is normally absent *e g* the arm thighs shoulder chest wall neck or the buttocks

The outstanding symptom is pain which may be extremely severe It may occur in spontaneous paroxysms (crises) or may be constant The patient is always on guard to avoid pressure on the structure The pain may spread over wide areas e g over the whole extremity Changes of temperature also cause pain Patients with the same structures but without pain are very rare (Lendrum and Mackey) Occasionally trophic disturbances are observed in the involved part of the body The finger containing a glomus tumor may be warmer and may flush or perspire Multiple tumors are occasionally seen Numerous instances have been reported in which the tumor appeared after a trauma in one patient shortly after the tip of the finger was crushed by the door of an automobile a glomus tumor appeared under the nail of this finger

The tumors are usually very small in size and measure only a few millimeters in diameter The measurements of one tumor however were 1 5×1 0×1 0 cm (Ottley) and in another the longest diameter was over 3 5 cm (Lendrum and Mackey)

Histologically the tumors show the characteristic structure of the normal glomus but the composition varies and individual parts of the glomus may be exaggerated Thus the tumors have been called angiomyoneuromas Masson differentiates between an angiomatous an epitheloid and a neuromatous tumor depending upon the tissue prevailing in the glomus structure

The tumors are not malignant They compress the neighboring structures and may cause circumscribed atrophy for example of the phalangeal bone Recurrence after incomplete removal of a tumor has been reported (Ottley)

Usually pain forces the removal of the tumor bringing complete cure The tumor is not sensitive to radiotherapy

PERNIO CHILBLAINS FROSTBITE IMMERSION FOOT

Apart from certain systemic reactions to cold characterized by profound shock or by paroxysmal hemoglobinuria there are several local syndromes to which brief reference should be made

Chilblains or pernio represent a mild inflammatory reaction developing after exposure to cold damp cold in particular They are related to trench foot a condition seen in soldiers whose feet are exposed to damp cold for several days This in turn is related to immersion foot which is encountered primarily in

survivors of shipwrecks when the feet have dangled in cold water for several days A somewhat similar syndrome has been described in men shipwrecked in tropical waters but in this instance other factors than cold are present

If cold is applied to the skin it leads at first to arteriolar constriction and then to marked hyperemia which is followed by itching swelling and wheal or flare formation due to the release of histamine like substances Very early often within a few hours vascular thrombi are formed from red blood cell debris which silts along the vessel There is some separation of the endothelium from the vascular wall Edema forms early Reactive inflammation blister formation ulcers and gangrene are found in more advanced or more severe cases

Cold is apt to produce effects where large areas of skin are supplied by relatively small vessels — the fingers toes nose and ears

Mild forms of this condition are rather common in adolescent women in temperate climates The lesions are situated above the malleoli the skin is tender when rubbed and swollen Many of these patients seem peculiarly sensitive to chilblains after a previous injury by cold and the burning itching tingling of pain may be associated with swelling from time to time Under these circumstances there may be some permanent alteration in the vessels or nerves that renders the individual susceptible to subsequent exposures to cold

In slightly more severe forms there may be scaling of the skin and even patches of gangrene which ultimately heal If the part is frozen edema and blister formation in addition to secondary infection precede necrosis or gangrene the dead part eventually sloughs off after a line of demarcation has formed

Those living in the Arctics do not suffer commonly from skin injuries consequent to exposure to cold Since they are fully aware of the dangers proper precautions are taken to avoid exposure In this connection it should be mentioned that exposure to cold involves a special danger in that lower temperature may produce local anesthesia and abolish the warning signals of impending freezing It is not the absolute temperature alone which is important but also the humidity of the air and the activity of the patient

Immersion foot may develop in a day or so after exposure The part is painful numbness and tingling is annoying There are no pulses in the arteries (Ungley et al) The swollen pallid skin contains cyanotic areas This is the so called prehyperemic stage Subsequently the pallor is replaced by erythema The feet become very warm but do not sweat Edema may obliterate the pulse which otherwise has become full again Pain is severe and continuous Vesicles containing straw colored or sanguinous fluid may form If local patches of gangrene develop they are usually not extensive and do not require more than amputation of toes The chief difference between frostbite and immersion foot consists in the fact that in the latter the tissues are chilled but not frozen

Until the last war it was recommended that the involved part of the body be kept cool and that only very slow thawing be permitted but since then it has been found that tissue damage is less when the involved extremity is warmed

as soon as possible The best temperature applied for thawing is around 40 C After thawing is completed warming is discontinued

Rubbing the affected area is forbidden since the entrance of infection into a blister abrasion or fissure may constitute a serious threat to life Pressure bandages tend to minimize the formation of edema Infection contributes greatly to the danger and must be controlled or prevented by measures which will not further injure the skin Therefore antibiotics should be given

The tropical form of immersion foot requires the additional management of vitamin deficiency and hypoproteinemia

Prophylactic measures prevent the appearance of chilblains and trench foot in most cases

DISEASE OF THE VEINS

Varicose Veins

Pathologic dilatation of veins may result from diffuse enlargement (phlebectasia) or unequal circumscribed dilatation (varicosities) While these phenomena may occur in the central nervous system the esophagus broad ligament urinary bladder spermatic veins and so forth reference will be limited to varices of the lower extremities

The actual incidence of varicose veins is unknown The usual estimate of 10 per cent in young healthy industrial workers is probably low since it concerns a selected group of adults

The etiology is equally obscure and it has been impossible to study the problem by animal experimentation The frequency of the disease in certain occupations (waitresses laundresses traffic policemen) that place a special burden on the legs and require the patient to stand for long periods is established The familial occurrence and the appearance in many members of the same family even in early youth emphasizes the significance of heredity A constitutional aspect is implied in the description of an asthenic type of individual with inherent weakness of the connective tissue The development of varices in the early stages of pregnancy before mechanical factors come into play suggests the participation of an endocrine influence the importance of increased abdominal pressure in the back flow of blood to the heart is demonstrated by the appearance of varicosities in patients engaged in hard labor

In general two factors a primary change of unknown nature in the vein wall and stasis seem to be of great importance

The early pathologic changes observed consist of dilatation elongation and tortuosity of the vessel associated with some hypertrophy An inflammatory reaction in and around the vessels is more or less constant but seems to be secondary to the stagnation of blood in sluggish pools rather than primary Thinning of the vein followed by saccular or spindle shaped dilatation begins near a valve and spreads distally Ultimately the continuous distention and perhaps infection lead to an infiltration of all layers of the vein by connective

tissue This rather characteristic fibrosis the genesis of which is entirely obscure may be followed by lime salt deposits (phlebosclerosis)

Symptoms The symptoms consist of fatigue of a drawing sensation and at times of pain Often these are early complaints evoking erroneous diagnoses This is particularly true when mere inspection does not permit recognition of the situation Sometimes there are cramps in the calves particularly at night or when the patient is in cold water Precordial pain dizziness and dyspnea occur because of pooling of blood in the lower extremities There is no parallelism between the extent of the varicosities and the number or severity of symptoms

Tests In order to ascertain whether the communicating veins function properly and are able to compensate for the abnormal circulation due to the varicosities certain tests are used In the Trendelenburg test the involved leg is elevated to empty the veins A tourniquet or cuff is applied about the upper thigh and the patient is allowed to stand If the veins remain empty or fill slowly (20—30 seconds) the test is considered negative if the veins fill rapidly (5—15 seconds) the test is positive In the latter instance the communicating veins are inefficient

Before undertaking any treatment to prevent the flow of blood in the superficial veins the physician should ascertain whether the deep veins are patent The simplest test is to apply an elastic bandage and ask the patient to walk Considerable discomfort appears if the deep veins are not patent

Perthes test is satisfactory for determining the patency of the deep veins The tourniquet is applied while the patient stands being placed just tight enough to prevent reflux from the saphenous vein The leg is then flexed and extended at the knee ten times or the patient may walk vigorously for a minute or two If the deep veins are patent and the communicating veins function normally blood is aspirated from the superficial veins and the varicosities collapse In the so called comparative tourniquet test the cuff is applied at different levels so as to determine the level at which the communicating veins are incompetent By this means one may demonstrate that low as well as high ligation is necessary If superficial *and* communicating veins are incompetent injections of sclerosing solutions are liable to be followed by recurrence of varicosities If only the saphenous vein valves are incompetent ligation followed by injections is usually not followed by a recurrence

In the Schwartz test the saphenous vein is percussed near its entrance into the femoral vein if the percussion wave is felt by the other hand which rests upon the varicose veins of the lower leg the valves are incompetent

Complications The complications created by varicose veins are numerous Besides thrombosis and thrombophlebitis a periphlebitis and suppuration may develop A varix may rupture externally or into the tissues The skin may become atrophic or pigmentation and eczema may appear when the varices have existed for a long time even elephantiasis may occur The notorious chronic varicose ulcer usually located on the inner side of the lower third of the leg may result from trivial trauma or may appear spontaneously These ulcers

are rarely painful but healing is associated with diffuse scar formation Edema of the ankle and leg is prone to develop if the patient stands for some time At any time an acute infection may occur with redness pain and increased swelling

Since the blood flows toward the periphery in a varicose vein pulmonary embolism is a rare occurrence following thrombosis

Varicose veins are almost useless for the circulation When the vein valves become incompetent the blood flows backward and toward the periphery in the varicosities The communicating veins alone conduct blood to the deep (femoral) veins which direct it to the heart The deep veins rarely become varicose owing to the support provided by the surrounding muscles they do however suffer not rarely from thrombosis and frequently are occluded when superficial varices are present If the communicating and the deep veins become affected and their valves become more incompetent intravenous and intracapillary pressure rises decidedly causing edema to appear This edema fluid is rich in proteins and leads to fibroelastic proliferation and induration Therefore one is justified in combatting it even with mercurial diuretics

Therapy In mild cases management should be limited to the application of an elastic bandage or the wearing of an elastic stocking

Formerly surgical procedures were the only method of treatment for marked varicose veins but later obliteration of the varix by injection became widely employed Recurrences are however common The method is based upon the fact that the intravenous injection of certain substances injures the vein wall to produce a phlebitis and local thrombosis with subsequent obliteration of the lumen Of the innumerable substances capable of producing an endophlebitis 5 per cent sodium morrhuate 15—30 per cent sodium chloride or 50 per cent dextrose are the most popular solutions they vary somewhat in efficiency the intensity of the local reaction and the amount of pain produced

The injection must be made with due regard for certain rules thus paravenous injection must be scrupulously avoided With many solutions meticulous care must be exercised since even a small amount in the paravenous tissues will result in a slough that may require excision and suture If there is any reason to suspect that some fluid has escaped from the vein novocaine should be injected immediately into the blanched area Moreover a bandage should be applied at the site of injection to lessen the chance of any leakage and to encourage adhesion of the vein walls With injections of sodium morrhuate anaphylactoid reactions occasionally occur particularly when a second series of injections is started after a rest period Unless the treatment is discontinued increasingly severe and even fatal reactions may occur A patch test has been advocated to determine sensitivity of the patient to the preparation

It is preferable to have the patient ambulatory except for a few minutes immediately after the injection this diminishes the possibility of embolism

There are many contraindications to injection therapy Among them severe cachexia advanced age, migratory phlebitis tuberculosis and the presence of intermittent claudication represent absolute contraindications equally impor

tant contraindications are a history of a cardiovascular accident hyperthyroidism and the presence of an acute infection of any sort

Injection therapy alone is done only when the Trendelenburg test is negative that is if the deep veins and communicating vessels are normal

Ligation of the saphenous vein and stripping of veins is a useful supplement when the valves of the saphenous vein are incompetent This is performed at the saphenofemoral junction and includes all tributaries of the saphenous at that point even if they are not dilated A similar operation is recommended in the presence of ulcers and brown indurated edema provided no infection is present Bed rest elastic bandages elevation and heat elastic adhesive dressings iontophoresis and numerous other procedures are available for the treatment of infected ulcers and should be employed before injection is undertaken

VENOUS THROMBOSIS AND THROMBOPHLEBITIS

Thrombosis

The importance of this process for the appearance of embolism its frequent occurrence and its dangers were discussed in a previous chapter A few further remarks seem relevant

Among the three factors regarded as responsible for thrombus formation — slowing of the blood stream chemical and physical alterations of the blood and injuries of the vascular wall — the first seems to be the least important Ligation of a vein at two points some distance from each other if done carefully to avoid endothelial damage causes a complete standstill of blood flow but no thrombosis Any trauma or surgical intervention may increase coagulability of the blood The susceptibility of patients with polycythemia to venous and arterial thrombosis is known The tendency of patients with fungus infections on the feet to thrombus formation was mentioned Dehydration also seems to be an established factor in increasing the likelihood of thrombus formation

Traumatic thrombosis may appear as late as 10 to 14 days after an injury The trauma may be trivial and often is forgotten by the patient A blow on the calf even by the relatively light object without the appearance of any visible alteration on the skin may cause a diffuse thrombosis of the deep veins Often the vein is not occluded by a thrombus but rather is compressed by fascia or an extravasal hemorrhage There is sudden sharp pain cyanosis and numbness

Heavy physical work may cause thrombosis of the axillary and subclavian veins with shoulder pain as well as cyanosis and edema of the arm (thrombose par effort) This accident is particularly common if the shoulder girdle is moved upward and backward without abduction of the arm Lifting a heavy object or pitching a baseball may cause this accident Injuries to the veins are common and may even cause them to rupture

Thrombophlebitis is more common in old age in carcinoma and in patients with varicose veins In rheumatic fever it occurs in the veins of the upper extremity and neck Aschoff bodies may be found in the walls of these veins

Prolonged sitting on poorly constructed seats may induce deep vein thrombosis. This was seen in the air raid shelters of London where the crossbars compressed the veins ("shelter legs"). Venous thrombosis occurs during flights in airplanes lasting for many hours. Compression of the calf veins by the weight of the leg in bedridden patients is thought to be responsible for the frequent occurrence of thrombi in these patients. On all these occasions mechanical compression of the veins may injure the endothelium and lead to thrombus formation.

In simple thrombosis, the symptoms are very few or absent or are elicited only by careful inquiry. Pain in the plantar area of the foot, calf pain on dorsiflexion of the foot were mentioned earlier. Spontaneous pain is found only in a circumscribed area. It may not be superfluous to stress again that pressure and massage should be avoided. The spontaneous pain may be a mere soreness or it may be excruciating, particularly if a thrombophlebitis with perivascular inflammation is present. In ileofemoral thrombosis, the pain may spread to the back.

It is estimated that deep vein thrombosis in the legs causes pulmonary emboli in one out of three cases. If these patients are ambulatory, walking upstairs may produce calf pain. Tenderness over the posterior part of the leg is almost always present. Swelling tends to be trivial and limited to the lower leg, but the thigh may be enlarged if the thrombosis extends to the femoral vein. The prophylaxis of venous thrombosis has been discussed earlier.

Venous thrombosis in the upper extremities is known as Paget Schroetter's syndrome. Males are usually affected. Among 300 instances, it was found on the right side in 60 per cent (Hughes). Swelling, pain, sometimes discoloration, paraesthesias, and overdistended veins are found. There is often local tenderness. Anticoagulants and cervical sympathetic block are used.

Thrombophlebitis

The local symptoms of thrombophlebitis vary considerably with the particular vein involved. The usual picture will be recalled by mention of the familiar extensive thrombophlebitis of the legs, phlegmasia alba dolens or milk leg of older writers. Pain is felt in the medial part of the thigh. Both lower extremities are swollen, pale, and somewhat colder than normal. There may be moderate tenderness along the course of the deep femoral vessels. The local picture will be modified if, as often happens, the thrombosis extends into the external and common iliac veins or even into the inferior vena cava.

Fever accompanies thrombophlebitis. There is a leukocytosis and an increase of the erythrocytic sedimentation rate. If the inflamed area is superficial, inflammation is evidenced by the presence of a warm, red area, but if deep veins are involved, the diagnosis may be difficult. Local signs are minimal or absent save for a small enlargement of the circumference of the calf if deep veins are affected.

The edema is partly due to increased capillary pressure Ligation of a large vein experimentally does not lead to edema and does not cause it clinically for there are too many collateral vessels If however many peripheral veins are obstructed edema develops This happens even in the absence of lymphadenitis and inflammation of the perivascular lymphatics Obstruction of major lymphatic trunks can however be a factor in the production of edema

The vasoconstrictor impulses arising from a thrombosed and inflamed vein cause arterial spasm and may even lead to gangrene (Homans) this is a common reason for the erroneous diagnosis of an organic arterial disease

Thrombosis of the veins of the upper extremities rarely causes pulmonary embolism In many cases the signs caused by pulmonary embolism lead to the diagnosis of pneumonia or pleurisy while the real situation is unrecognized

Perlow described as phlegmasia caerulea dolens a syndrome with shock and unconsciousness caused by the loss of about 5000 ml of plasma into the tissues There is severe cyanosis of the leg with petechiae and purpura Blood and plasma replacement may be life saving

Therapy In venous thrombosis and thrombophlebitis the local excruciating pain is often ameliorated by the application of three or four leeches in the neighborhood of the thrombosed vein area The treatment is ridiculed only by those who have never tried it in our experience the results have been very gratifying

In thrombophlebitis of the lower leg bed rest is indicated when acute inflammatory symptoms are present The inflammatory process subsides more rapidly by immobilization and the edema diminishes as the result of elevation Decrease of the edema is important since it tends to be a permanent feature if it persists for any length of time Restriction of fluids and of salt as well as the use of mercurial diuretics or calcium gluconate have been advocated to lessen edema formation The use of novocaine block to relieve veno and arterio spasm which are likewise considered important factors in the production and maintenance of edema is mentioned below

A difficult problem always faced is the duration of bed rest No standard period is known Prolonged recumbency offers just as much danger as premature walking The former may lead to the formation of new thrombi the latter to pulmonary embolism Unfortunately no reliable method is available to decide the best course in a given case In thrombosis of the femoral and pelvic veins bed rest must be prolonged four to five weeks The foot of the bed is put on blocks The patient is admonished to avoid deep breathing and straining at stool

Many physicians do not advocate bed rest at all unless acute inflammatory symptoms are present In our experience if there is much pain walking in the early stage of the disease greatly aggravates the swelling since the collateral veins and lymphatics are incompletely developed

For the arterial spasm paravertebral injection is beneficial and has been widely used since Leriche s recommendation It relieves pain and as mentioned

above edema It also restores arterial circulation If the sympathetic trunks are to be blocked this measure should be instituted early and should be repeated a few times

If pulmonary embolism is present and its recurrence seems likely, femoral vein ligation has been performed just distal to the entrance of the saphenous vein Some operators prefer to divide this vessel hoping thereby to interrupt impulses responsible for the vasospastic effects Even the inferior vena cava may be ligated if one has the impression that both femoral veins are thrombosed or if there is a thrombosis of the iliac vein The operation does not absolutely prevent the occurrence of embolism but greatly diminishes the risk These operations have been known to gynecologists for many years and were employed successfully in cases of gynecologic sepsis

If operations are performed in patients whose collateral pelvic veins are also occluded serious complications will follow

Therapy with anticoagulants is the method of choice and gradually replaces venous ligation This was discussed in the section on pulmonary embolism It is applicable in thrombophlebitis as well as in thrombosis

The value of trypsin given intramuscularly is still not established (Innerfield) Stein warmly recommends therapy with phenylbutazone

Chronic edema of the leg consequent to a femoral vein thrombophlebitis is often followed by persistent induration of the skin and subcutaneous tissues Subsequently pigmentation appears and the leg ultimately turns brown The indurated tissue does not pit on pressure but ulcers are prone to occur Pain is variable and at times very annoying Infection of the lymphatics and extravasation of serum containing large amounts of protein leads to the deposition of scar tissue which contributes to the blockade of veins and lymphatics The treatment of this complication requires limitation of activities avoidance of dependent position of the legs and the application of elastic bandages unless further measures are indicated for the ulcers Examination from time to time may disclose soft areas that may contain large varices demanding injection therapy

THROMBOPHLEBITIS MIGRANS

Thrombophlebitis migrans or migratory phlebitis is a painful phlebitis and periphlebitis which occurs mostly in males Short segments of veins usually 5—10 cm in length are affected The involvement is usually observed in subcutaneous veins but in rare cases the deep veins are also affected Every recurrence is accompanied by an increase of temperature general disturbance of well being and tachycardia The affected superficial veins are palpable as hard tender cords which show at first a light red color then a livid discoloration and finally a brownish hue The inflammation also involves neighboring tissues for a distance of 3—4 mm from the vein

Widely separated areas are affected One day a painful thrombosis of a short section of a foot vein appears On the next day week or month another

vein is involved at the elbow on the inner side of the forearm or in the neck Thrombosis may even spread into the cranial venous sinuses Most cases described as thrombosis of the coronary or pulmonary veins with angina pectoris were actually instances of pulmonary embolism These with all their manifestations and complications are not unusual in thrombophlebitis migrans

In an astonishing number of cases focal infection is observed and the process disappears when these foci are successfully eradicated Histologically a periphlebitis and thrombophlebitis similar to that seen in thromboangiitis obliterans is noted For some authors every case of thrombophlebitis migrans is simply a form of Buerger s disease although we do not share this opinion The arterial circulation should be watched carefully in every case of migratory phlebitis

The course may be protracted and the disease may last for decades In some cases observed by us the progress was stormy and hyperacute In a few weeks multiple emboli may lead to death On the other hand the process may disappear at any time

In a large number of cases migratory phlebitis accompanies carcinoma It has been repeatedly described as an early sign of pancreatic carcinoma We have seen it early in ovarian and gastric carcinoma The relationship is obscure In pancreatic carcinoma a relation may exist to the mucin production (Durham) Thrombophlebitis migrans was observed to disappear after surgical removal of the carcinoma

The therapy of choice is the administration of anticoagulants which must be continued for months Oral administration of butazolidine (phenylbutazone) has been recommended Three and one half grams are given in one week (Stein)

Occlusion of the Superior Vena Cava

More than half of the cases of compression of the superior vena cava result from aneurysm of the aorta Another 25 per cent originate from carcinoma of the bronchi Thrombosis of the superior vena cava possibly the result of a phlebitis of unknown origin is sometimes seen in tuberculosis syphilis or pyogenic infection Occurring in cardiac patients with advanced decompensation it usually starts in the jugular veins and is propagated into the superior vena cava We observed it in one patient with thrombophlebitis migrans

Although thrombosis of the superior vena cava may occur at any age it seems to be most common in the fifth decade Nearly two thirds of the patients are males

The pathognomonic symptoms and signs are edema and cyanosis of the face neck and upper extremities aggravated in the recumbent position and relieved in the erect posture The venous pressure is increased in the arms while pressure is normal in the lower extremities Dilated collateral veins may be visible on the anterior chest wall within a short time The slow cerebral circulation may lead to dyspnea and hyperventilation Pleural effusion may develop as the result

of increased pressure in the azygos veins Headache aggravated by lying horizontally is not uncommon vertigo may be noted Somnolence is an occasional symptom Prominence of the eyes and staring may be conspicuous Tinnitus and deafness may occur but vanish with the development of a collateral circulation

The symptoms depend to a great extent both upon the rapidity with which thrombosis develops and the underlying disease If the former proceeds slowly and collaterals form rapidly many symptoms like cyanosis facial edema and so forth may be absent

The prognosis depends partly upon the associated disease and partly upon the relative rates of venous occlusion and the development of a collateral circulation The mortality rate is high Death usually occurs in a few months but survival for many decades is possible In one personally observed case the thrombosis followed an acute tonsillitis this patient was still alive after six years although he suffered from extreme vertigo when his position was changed suddenly We have seen tuberculous endophlebitis of the superior vena cava with occlusion unfold its picture in a matter of weeks sometimes there is a marked change of personality before death

In recent years surgery has provided great relief to patients with this syndrome The azygos vein has been grafted into the right atrium or with the aid of arterial grafts it has been anastomosed to an innominate vein and patent parts of the superior vena cava

Occlusion of the Inferior Vena Cava

A thrombosis or thrombophlebitis in the course of an infectious disease occasionally causes an occlusion of the inferior vena cava More often this event is due to a thrombus propagated from another vein Most common in our experience is occlusion of the inferior vena cava by a renal new growth in which a large mass of neoplastic tissue ascends the inferior vena cava

When occlusion of the inferior vena cava complicates the terminal phase of some other disease the clinical picture need not be modified When symptoms develop at all they consist mainly of leg edema and edema of the back without ascites The urinary output may diminish Subsequently an extensive collateral circulation may develop in which the superficial veins of the abdominal wall participate However we have observed collateral circulations in which the deep veins of the abdominal wall alone acted vicariously for the occluded vena cava and the diagnosis was impossible since no collateral circulation was visible externally

Among the measures for symptomatic relief repeated venesection may possess great value It may not prolong life but it may relieve many annoying symptoms for 48 hours or more

From the standpoint of differential diagnosis the principal source of confusion has been to mistake occlusion of the inferior vena cava for Baumgarten's

syndrome of the paraumbilical veins In both a remarkable caput medusae may be present but otherwise there is little similarity The outstanding signs of Baumgarten s syndrome apart from the caput medusae and thrill is splenomegaly and at least in many cases the recurrent ascites moreover Baumgarten s syndrome in our experience is seen in young individuals of the asthenic habitus who frequently lack secondary sex characteristics

Suppurative pylephlebitis and its relationship to appendicitis and to liver abscess endophlebitis syphilitica of the hepatic veins (Chiari s disease) splenic vein thrombosis and its association with the Banti syndrome various types of portal vein thrombosis and particularly the relatively common form observed in connection with cirrhosis of the liver as well as many other di eases of the veins belong to the domain of Internal Medicine and are not discussed in this volume

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Chapter 31

Therapy

General Remarks

In this chapter some measures available for the treatment of cardiac diseases are reviewed A large number of therapeutic procedures for special conditions have already been discussed in the preceding individual chapters The agents serving especially for the management of cardiac failure will find consideration in the discussion which follows

Cardiac failure and decompensation should not be treated exclusively with drugs Rest and appropriate diet alone will restore compensation in many patients

The method of treatment so popular in the past consisting of complete digitalization and then dismissal of the patient until cardiac failure reappeared has been properly abandoned Such treatment can be compared to leaving a non swimmer under water and lifting his head out of the water now and then to prevent complete asphyxia The patient must be under continuous control his activities must be planned and discussed in detail with him Compensation must be maintained by the mode of living as well as by continuous administration of drugs

When decompensation develops an endeavor should be made to determine its cause Knowledge of the precipitating factor helps greatly in treatment Often the appearance of an arrhythmia particularly atrial fibrillation of an infection with hemolytic streptococci pulmonary embolism extra physical strain or undernutrition will precipitate cardiac failure In all these instances it is possible for the situation to improve after the disappearance or elimination of the precipitating factor After they have recovered from cardiac failure these patients may have an efficient and fully compensated circulation for years

Decompensation must be considered much more grave however if it develops from failure of a markedly dilated heart or a steadily progressive process such as coronary sclerosis Under these circumstances there is not much prospect that the state of the patient will remain satisfactory without continuous treatment But even in the latter instance decided improvement may occur if in the case of an earlier infarction collateral circulation develops and strong scars are formed in the myocardium Therefore even the symptoms and signs of advanced cardiac failure in coronary sclerosis should never lead to an absolutely poor prognosis

Psychotherapy has considerable importance in the management of decompensated patients and should not be neglected All encouraging features should

be stressed such terms as cardiac failure should be avoided in discussion with the patient The term congestion is less alarming The importance of preventing mental strain and nervous tension in patients with hypertension or coronary thrombosis was mentioned in the respective chapters

The removal of visible edema dyspnea or tachycardia is not the ultimate objective of therapy Many weeks of treatment sometimes are needed until the heart acquires sufficient reserve and the patient is in an optimal condition The disappearance of dyspnea or edema does not constitute the maximal benefit from treatment

A discussion of the sexual life of the patient ought not to be omitted becau e of a false sense of prudery Actually patients are often thankful that they were anticipated in this question which they may have hesitated to raise In ca es of coronary disease many deaths during sexual intercourse could have been prevented if the patient had been told to take nitroglycerin before the act

Greatest attention should be devoted to the treatment and prevention of all infections It was shown in the chapter on myocarditis how often the heart muscle is involved in various infections Patients with advanced valvular lesions or severe hypertension remain compensated for years as long as the heart muscle is normal but the slightest impairment of the myocardium may lead to cardiac failure It is readily conceded that dental granuloma gingivitis and dental ab ce ses do not play the role ascribed them by some advocates of the doctrine of oral sepsis Nevertheless foci of this kind possess great and often underestimated significance in many cases

Medicine possesses no satisfactory test for estimating the functional capacity of the heart and none for the early diagnosis of decompensation All the innumerable tests described such as registration of the heart rate and the re piratory rate the blood pressure at rest and after measured work and all the recommended combinations of these tests have little value The least exertion may increa e the pul e rate and blood pressure more in the otherwise healthy neurotic individual than in a decompensated patient A careful history and exact examination furnish much more information on the state of the circulation of the patient than any of the functional tests now available

DIGITALIS

No other drug employed in medicine has created a literature as voluminou as that of digitalis Numerous monographs and innumerable experimental and clinical papers have digitalis as their subject While much research has been done particularly in recent years on digitalis glycosides and on purification of the drug the clinical rules laid down by Withering still hold and have been little improved This does not reflect adversely on the scientific zeal of workers in all countrie but merely proves how unusual the experience the excellent powers of observation and the remarkable descriptions of Withering

Chemistry

Among the many plants of the digitalis group the leaves of digitalis purpurea and of digitalis lanata are used almost exclusively at present as the source of digitalis preparations Digitalis lanata is a species of foxglove that has the advantages of easy cultivation and a large content of active glycosides

The digitalis glycosides are composed of an aglucone (genin) fraction and a sugar fraction The latter is important for the solubility of the glycoside and enables it to penetrate the cells The aglucone fraction has a phenanthrene structure similar to that of the sex hormones (sterols) and desoxycorticosterone and exerts the specific cardiac effect

The three glycosides isolated from the leaves of digitalis purpurea — digitoxin gitoxin and gitalin — are known to have precursors they are not genuine glycosides (Stoll) These have still not been isolated

From digitalis lanata three products digilanid A digilanid B and digilanid C have been isolated from these digitoxin gitoxin and digoxin are derived

Digitalis contains many other substances among them the saponins which promote absorption from the gastrointestinal tract

The isolation of pure crystalline products digitoxin from digitalis purpurea (digitaline Nativelle isolated as early as 1869) digoxin (isolated by Smith in 1930) and cedilanid from digitalis lanata makes possible the administration of pure products of known strength

Pharmacology

Action of the Heart Muscle Digitalis glycosides increase the contractility of the myocardium This is seen even in isolated muscle strips and may also be observed microscopically in fibers from the specific tissue Systole is strengthened and is more complete so that the heart empties better The heart muscle is enabled to overcome greater resistence and its absolute power is increased The minute volume may be doubled There also are some effects on the diastolic phase although they are not very pronounced in the mammalian heart The speed of relaxation is increased but diastolic size is not reduced The increased velocity of the contraction shortens the duration of systole and the refractory phase (Junkmann) The pump works quicker stronger and the piston of the pump goes deeper than before digitalization

The action of digitalis on actomyosin and adenosine triphosphate is not clear It is possible that the diminished amount of ATP (Wollenberger) in the heart of patients with thiamine deficiency or hyperthyroidism explains the poor effect of digitalis in these conditions Digitalis increases the glycogen content of the heart muscle and diminishes the amount of lactic acid According to Pothlin et al digitalis interferes with energy utilization and not with energy production Bing et al found that strophanthin does not affect oxygen consumption of the failing heart which remains normal According to Proctor et al digitalis influences the enzyme systems that regulate the level of adenosine triphosphate

In patients with heart failure digitalis leads to disappearance of congestion diminution of residual blood fall of atrial pressure lower venous pressure better nutrition of the tissues and finally to an increase of the cardiac reserve power The peripheral blood depots open partly due to the disappearance of edema and partly due to widening of the peripheral vessels by other mechanisms All these actions begin soon and bring about a remarkable improvement It is claimed that digitalis is ineffective in high output failure This is true in our opinion only if the causative factor (pulmonary pathology arteriovenous fistula etc) persists in great intensity

Action on the Vagus Digitalis glycosides increase the vagal inhibition of the heart This effect is not of central origin it has been explained by increased sensitivity of the receptors in the carotid sinus (Heymans et al) or by sensitization of the heart muscle to the (normal) vagal tone (Abdon and Nielson)

This heightening of vagal inhibition is beneficial It may slow the heart particularly in cases of atrial fibrillation where it slows the ventricles by inhibiting the atrioventricular conduction The contractility of the ventricles is not impaired by this vagal action since — as was pointed out before — there are no vagus fibers and therefore no direct vagal effects on the mammalian ventricle

The conduction of a stimulus over the heart is directly impaired by large doses of digitalis This effect is observed even in isolated muscle strips

Action on Blood Vessels Much has been written about the vascular effect of digitalis glycosides A general vasoconstriction particularly in the gastrointestinal tract seems to take place under certain conditions but not with doses comparable to those used in therapeutics This effect is also counteracted by the improved peripheral blood supply the result of the stronger and shortened systole The special situation of the coronary arteries will be discussed later

There is no proof of a direct diuretic effect on the kidneys Any increase in urinary output is the indirect consequence of the improvement of circulation

Action on the Normal Heart It is often maintained that digitalis does not affect the normal heart but this statement is certainly untrue It must be expected that the efficiency of the systolic contraction will not be remarkably increased if the heart works under normal conditions The minute volume cannot increase as long as the inflow of blood to the heart remains the same If toxic doses of digitalis are given to healthy individuals the minute volume falls a finding that could be anticipated in view of the toxic effects of large doses of digitalis on the heart muscle According to some authors the diminished output is due to peripheral factors (Dock and Tainter)

Fixation and Cumulation Digitalis is fixed in the heart (Hatcher) It is still present 28 days after administration of one large dose It has been estimated that the heart loses daily 3 to 7 per cent of the cumulative amount of digitoxin The binding of scilla and strophanthin is slight Friedman et al found that the renal excretion of digitoxin lasted 24 days It is significant that elderly patients excrete much smaller amounts

The digitalis glycosides cumulate Even very small doses may suddenly exert toxic effects when repeated often over a sufficient length of time Originally cumulation was explained by simple addition until it was shown that large sublethal doses of digitalis cause necrosis of the myocardial fibers This necrosis was seen first in 1904 but was completely forgotten until it was rediscovered in recent times It is not yet decided whether the necrosis is caused by a direct action of the digitalis on the myocardium or whether it is due to ischemia Digitalis in sublethal doses also causes hyaline necrosis in the aorta and in the walls of the renal and coronary arteries Degenerative changes have also been seen in the brain The necrosis and hyaline degeneration in the myocardium is situated around the papillary muscles in particular it is followed by secondary leukocytic infiltration We may assume that smaller doses of digitalis alter the myocardial cell without leading to histologic changes It is probable that the cumulation is due to the increased sensitivity of the myocardium altered by small doses of digitalis to additional doses

The heart was supposed to store more digitalis than any other organ However recent investigations with the embryonic duck heart as test object (Friedman et al) speak against this predilection The authors found the greatest concentration in the liver and kidneys It is interesting to note that the tissues of the rabbit (examined by Friedman s technique) do not retain digitalis as compared to the tissues of other animals Digitalis is fixed by the cat heart but not by the rat heart and even the cat heart does not fix more than other organs of this animal This should be a warning against drawing conclusions from one species to another

The maximum capacity for destroying digitalis is according to Friedman et al 50 micrograms daily This amount is the same whether 0 1 or 0 2 mg of digitoxin are given

Most of the digitalis administered is excreted by the urine (80 per cent) and feces in an inactive form Only traces of active substances are excreted

Using radioactive digitoxin Okita et al found minute amounts in the heart after 40 days

Electrocardiogram The digitalis glycosides cause visible effects in the electrocardiogram *The shortening of systole can be measured in the electrocardiogram* and may amount to 41 per cent (Berliner) Within a few hours a single large dose may depress the PS T segments and lower the T waves These changes may persist for more than three weeks after discontinuation of treatment (figure 114) Extrasystoles will be discussed later Digitalis also causes atrioventricular conduction disturbances In some hearts with a damaged myocardium they appear following small doses

In figure 115a a prolonged P P interval exists The tracing was obtained from a 56 year old patient with hypertension who had received 0 3 Gm of digitalis daily for 18 days in the form of tablets of powdered leaves The P P interval measured 0 32 second In lead I the third atrial stimulus is not conducted to the

ventricle the following conduction is shorter due to partial recovery (Wenckebach's period) The RS-T segments and T waves are displaced in a direction opposite to the main deflection—a typical digitalis effect. Figure 115b was

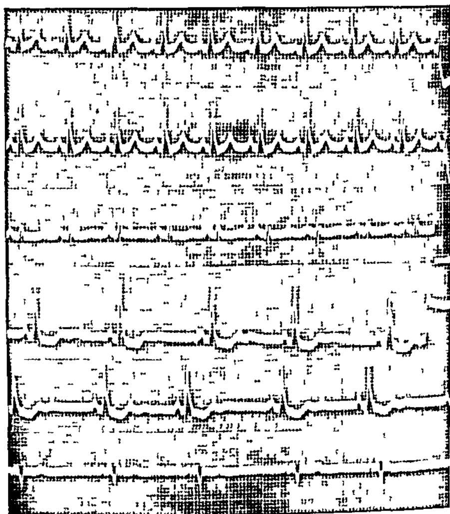
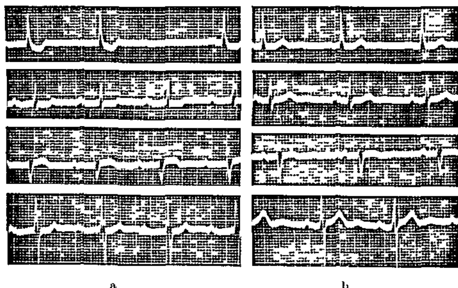


FIG 114 The upper three strips represent the three standard leads before, the lower 3 strips after digitalis therapy. *Note the change of rate* and the depression of the RS-T segments with lowering of the T waves. U waves appear; this is common and may be explained by the diminished content of potassium in the heart muscle.

taken from the same patient 17 days after digitalis had been discontinued. The digitalis effects (conduction disturbances, shortening of systole and RS-T changes) have disappeared.

Standardization. Methods for standardization of digitalis according to the amount necessary to cause standstill of the frog or cat heart in a given time

under certain experimental procedures are in wide use One should not forget however that preparations having the same strength experimentally (containing the same number of cat units) may have a quite different activity in men Even cat units cannot be compared with each other *because of different methods* used Likewise they cannot be compared to frog units since preparations having the same number of frog units may have different toxicity when tested in cats Therefore the labels indicating standardization of a preparation on frogs or cats may be somewhat misleading They often give a false sense of



a b

FIG 115 Atrioventricular block and deformation of the RS T segments and T waves caused by digitalis (a) Only left axis deviation remains 17 days after digitalis was discontinued (b)

security in dosage In a similar way standardization in man which has often been tried encounters great difficulties

Many preparations particularly tincture of digitalis *deteriorate rapidly* The pure glycosides do not require bioassay

Indications

Scientific evidence and reasoning often only superficially accurate cannot yet be conceded the final argument for or against the administration of digitalis in a special case The dose and mode of treatment must be determined by the real benefit the patient derives from it A long life is too short to learn enough about this wonderful drug (Wenckebach)

These sentences written by a great cardiologist illustrate clearly the superiority of practical experience over theoretical knowledge in digitalis treatment

Digitalis therapy is a great art that cannot be learned from books Only the inexperienced take it lightly Lives may be saved or astonishing improvement may be accomplished by a slight increase in dosage the addition or decrease of one tablet of 0 1 Gm of digitalis per day may change the whole picture

An exact knowledge of the indications and contraindications is the necessary basis for any therapeutic program with digitalis

There are two main indications for the treatment (1) evidence of cardiac failure (2) arrhythmias particularly atrial fibrillation with too rapid a ventricular rate

Cardiac Failure In the presence of rhythmic cardiac action evidence of myocardial failure is the only indication for digitalis Cardiac failure is evidenced not only by edema dyspnea and engorgement of the liver but also by Cheyne Stokes respiration nocturnal cough hydrothorax and pulmonary congestion Digitalization should not be postponed until cardiac weakness has fully developed The drug should be given at the first sign of myocardial failure

It has been stated that digitalis never helps patients with rhythmic cardiac action unless hypertrophy of the heart exists in combination with dilatation (Edens) Although no proof can be cited to support this statement there is some truth in it In concentric hypertrophy alone digitalis is not indicated and no help can be expected from it since the heart is not decompensated and no failure exists In patients with pure dilatation as in a case of toxic myocardial damage or following unusual strain digitalis is useless Digitalis is also useless in the myocardial necrosis of diphtheria and coronary sclerosis and in the myocardial damage of rheumatic fever Only if the basic condition or another disease in these cases (hypertension chronic coronary artery disease) has already led to hypertrophy and dilatation does the drug improve the condition of the patient

Digitalis is of course useless in congestive failure caused by pericarditis or cardiac tamponade Only in slowly developing myocardial failure as it actually happens in the majority of decompensated cardiac patients in whom hypertrophy and dilatation of some part are combined is digitalis useful

Digitalis is administered to these cases primarily for its positive inotropic effect that is to improve the contractile power of the heart muscle

In the presence of rhythmic cardiac action slowing of an accelerated cardiac rate (sinus tachycardia) by digitalis is often impossible If the tachycardia is caused by decompensation (Bainbridge reflex) it may disappear during digitalization (figure 114) but in many cases it persists unless toxic doses are used Thus in mitral stenosis with regular sinus rhythm and sinus tachycardia the rate remains rapid even if large doses of digitalis are administered In those patients who also exhibit marked pulmonary congestion digitalis is of little or no value because it does not help overcome the valvular defect and neither ventricle is incompetent Sometimes a tachycardia has a compensatory effect to maintain cardiac output as pointed out before

An increase of rate alone need not be the occasion for inaugurating digitalis therapy since cardiac acceleration occurs in the absence of decompensation

Thus considerable tachycardia may be encountered in a cardiac neurosis in hyperthyroidism in patients with aortic regurgitation in endo and myo carditis and other conditions without coexisting decompensation Often an entirely superfluous digitalis therapy is initiated in these patients It is on the other hand well known that digitalis often restores compensation without slowing the heart

Occasionally digitalis is withheld from decompensated patients even when they suffer nightly from attacks of paroxysmal dyspnea simply because the cardiac rate is slow One may encounter severely decompensated patients in whom the cardiac rate does not exceed 60 to 70 beats per minute Not rarely this happens to patients with coronary sclerosis in whom this bradycardiac decompensation may be due to abnormal nutrition of the sinus node It occurs in aortic stenosis The hesitancy to give digitalis in these patients is not justified The heart rate in these patients does not become slower during digitalis treatment and digitalization will cause marked improvement

Arrhythmias The second indication for digitalis therapy is seen even in the absence of cardiac failure it is represented by cases of atrial fibrillation and a rapid ventricular rate Here as pointed out before engorgement of the liver venous congestion and edema appear early when the ventricular rate is high In these cases impairment of conductivity by the direct action of digitalis on the specific tissue and via the vagus slows the ventricular rate to values between 70 and 80 beats per minute As soon as this level is reached the circulation is in an optimal condition Since with rare exceptions slowing occurs regularly with the employment of relatively small doses these patients react exceedingly well to digitalis Only a slight impairment of conductivity is necessary to prevent the majority of the weak stimuli originating in the fibrillating atrium from reaching the ventricle In rare cases atrial fibrillation may disappear during digitalis treatment even rarer are patients in whom the onset of fibrillation coincides with the treatment The special method of treating atrial flutter with digitalis has been discussed earlier

Other arrhythmias such as atrial extrasystoles and paroxysmal tachycardias are also abolished by digitalis but they respond better to other drugs e g quinidine

Other Indications Apart from the group of patients presenting cardiac failure and those with atrial fibrillation and flutter there are only rare indications for digitalis One is mentioned below in connection with heart block

The administration of digitalis in infectious diseases or preoperatively in order to strengthen the heart has been properly abandoned In these conditions peripheral circulatory failure rather than cardiac failure develops occasionally and digitalis is useless The administration of digitalis in pneumonia in the pre antibiotic era was abandoned after it was shown that there was no proof that routine administration of digitalis in these cases lowers the mortality It has also been recognized for a long time that cardiac weakness is not responsible for shock in this condition digitalis is therefore often without value

Contraindications

The contraindications to digitalis since they are so few may be summarized briefly Our claim that such contraindications are practically nonexistent is based on the fact that whenever the administration of digitalis is necessary it *must* be carried out since there is no substitute If cardiac failure is present or if the ventricular rate is too high in atrial fibrillation therapeutic success is not obtained without digitalis and the condition of the patient steadily deteriorates unless it is given Naturally there are patients in whom large doses of digitalis must be avoided but no contraindication to digitalis is admitted Allergy or intoxication signs mentioned below occasionally prevent continuation of treatment

For obvious reasons digitalis will not help in congestion of the liver and veins in pericardial diseases or cardiac tamponade nor will it abolish dyspnea due to pulmonary disease Even in patients with mitral stenosis and pulmonary congestion with sinus rhythm digitalis is not indicated and is useless

Since some older textbooks enumerate an entire series of contraindications they must receive some mention in this section

Paroxysmal Ventricular Tachycardia This disturbance — contrary to prevailing opinion — is a contraindication to digitalis therapy only when it appears during the administration of digitalis and is elicited by it Attacks of ventricular paroxysmal tachycardia not induced by digitalis are no contraindication and in fact respond favorably to it Thus we saw success in ventricular tachycardias following acute myocardial infarction even when quinidine was ineffective Scherf and Kisch observed a patient with attacks of ventricular tachycardia with alternating forms of ventricular complexes that always disappeared when digitalis was given

High Blood Pressure A warning was issued against digitalis therapy in the presence of an elevated blood pressure owing to the alleged danger of a further rise during the course of treatment The improved contractility and the shortening of the systole actually should lead to an increase of systolic blood pressure However so many regulating factors influence the level of the systolic blood pressure that at the bedside its height can always be disregarded in the question whether digitalis is necessary Often in decompensated hypertensive cardiac patients the blood pressure even falls during the course of the treatment of hypertension if decompensation was the cause of the hypertension (stasis hypertension) In other cases the blood pressure increases during digitalization But in these instances hypertension was present for a long time during the period of failure the blood pressure dropped but rose once again as digitalis therapy improved ventricular contractility

Embolism Patients who recently experienced an embolism in the lesser or greater circulation were often considered unsuitable for digitalis because of the fear that more powerful contractions of the heart induced by the drug might lead to the release of more thrombi and cause further embolism Any increase of

cardiac action due to a rapid movement or unavoidable excitement naturally offers the same danger Furthermore in these cases as in all others digitalis is given only when indicated therefore it must be administered since there is no drug with a different mode of action that can replace it

Coronary Disease Many physicians withhold digitalis from patients with angina pectoris and myocardial infarction In patients with anginal pain the detrimental effect due to narrowing of the coronary arteries is considered dangerous while in myocardial infarction rupture of the heart the result of more powerful contractions after digitalis is considered possible

Despite a tremendous amount of experimental work concerning the effect of digitalis (and strophanthin) on the coronary blood flow no decisive results have been obtained This is largely due to the fact that the coronary blood flow during digitalis therapy is influenced by factors which in many respects act oppositely The increase of cardiac contractility with shortening of the systole and the change of the heart rate may improve coronary blood flow while the increased vagus tone may diminish it A direct action of digitalis on the coronary vessels can only be studied in experiments on excised isolated vessels According to some investigators toxic doses narrow the coronary vessels No effect or only negligible reduction of blood flow is reported by others

Large doses of digitalis were given to 15 patients with angina pectoris and a positive exercise test i e marked changes in the electrocardiogram on exertion and in only one case did the complaints slightly increase in this single instance the alterations in the electrocardiogram became more pronounced on exertion after digitalis therapy (Hauser and Scherf)

Clinical experience shows that digitalis should be given if indicated to patients with angina pectoris due to coronary stenosis or patients with myocardial infarction

In cases of angina pectoris on effort the attacks occasionally disappear during the period of decompensation and reappear once compensation is restored This fact well known for many years has been questioned recently We have observed it repeatedly particularly in cases of aortitis and angina pectoris due to coronary stenosis The physician faces a dilemma and must choose between the Scylla of angina pectoris and the Charbydis of cardiac failure The disappearance of angina on effort in decompensation may be accounted for by the diminished activity of the patient due to dyspnea, edema and so forth But the fact that anginal pain at rest may also disappear has not as yet been satisfactorily explained

In coronary thrombosis with myocardial infarction the appearance of pulmonary congestion alone especially in the first few days is no indication for digitalis One will often succeed in preventing pulmonary edema and abolishing dyspnea by means of small doses of morphine and the congestion will disappear within a few days If however the signs of congestion increase despite morphine or if gallop rhythm and other signs of myocardial damage appear digitalis must be given The effect here often is as miraculous as in other cases Digitalis may

be particularly necessary in patients with a second or third attack of myocardial infarction or patients with chronic hypertension who develop myocardial infarction

Heart Block Cases of heart block (atrioventricular block) are often cited as unsuitable for digitalis therapy because of the danger of further cardiac slowing If complete atrioventricular block is present this fear is groundless since digitalis does not reduce the automatism of the ventricular centers but rather augments it if proper dosage is used Accordingly patients with heart block and a ventricular rate even as low as 20—30 may be digitalized without danger In patients with an incomplete heart block digitalis therapy may lead to a complete interruption of the atrioventricular conduction This event represents a lesser evil than non digitalization of a failing heart In fact digitalis is prescribed in atrial fibrillation for the purpose of impairing atrioventricular conduction and producing heart block Therefore cautious administration of digitalis in cases of heart block is permissible and even indicated when continuous change from partial to complete A V block causes Stokes Adams attacks

Signs of Intoxication and Side Effects of Digitalis Treatment

While true contraindications to digitalis treatment do not exist in some cases the administration of the drug must be interrupted even if its continuation seems indicated Interestingly enough many of these signs of intoxication and side effects of digitalis therapy were known to Withering

Allergy The administration of digitalis is sometimes impossible because of allergy to the drug Instances of scarlatiniform rashes urticaria asthma pruritus edema of the face and fever caused by digitalis have been described Rarely we have also seen skin rashes appear during the administration of strophanthin

Nausea and Vomiting Digitalis vomiting is not the result of direct irritation of the gastric muscosa since vomiting occurs on parenteral administration nor is it due to irritation of the vomiting center Some investigators considered reflexes emerging from the heart and running predominantly over the vagus responsible while others assumed that reflexes from the liver or other abdominal viscera cause it Vomiting has been observed however even after extensive severance of connections between the heart and the abdominal organs from the central nervous system Digitalis is said to have a central emetic effect which summates the effects caused by stimulation of peripheral reflexes outside the intestine (Borison) The oral administration of galenic preparations may cause direct irritation of the stomach by virtue of the saponins and other ballast substances

The vomiting often comes in waves with periods of relative wellbeing between them

If vomiting occurs during the course of digitalis treatment one possibility should always be considered namely that the doses administered are too small

to control the failure and the vomiting is due to hepatic enlargement and congestion This type of vomiting naturally vanishes if therapy is continued with adequate doses of the drug

Digitalis vomiting does not depend solely on the dosage It occurs in some patients even after small amounts of digitalis while in others relatively large amounts fail to induce it Therefore one is not permitted to consider the appearance of vomiting as a sign that the patient is fully digitalized

Anorexia nausea and diarrhea may also occur

Salivation Fatigue and Other Signs Neuralgic symptoms with shooting pains tingling of the fingers and generalized muscular pains have been described (Batterman and Gutner) Delirium may appear (Duroziez King) caused by injury to nerve cells Gynecomastia is found because of the action of the aglucones (LeWinn)

Other untoward effects described by Withering are increased salivation and great lassitude The latter appears particularly in elderly patients who also suffer occasionally from headaches delirium hallucinations and convulsions

Visual Disturbances Green and yellow vision is common blue and red vision is rare Dimness of vision inability to focus scotomata and even temporary blindness are occasionally observed

Eosinophilia A marked eosinophilia appears in the blood in some patients allegedly through an increase of vagal tonus (Pecht Romano and Geiger) Up to 30 per cent eosinophiles have been observed during digitalization

Anuria Anuria due to digitalis is rare but undoubtedly occurs In one of our patients with lead poisoning hypertension and nephrosclerosis the administration of four tablets of 0 1 Gm digitalis daily led to oliguria and water retention After the drug was discontinued for 2 or 3 days there was a profuse diuresis and a weight loss amounting to 5 Kg The experiment was repeated a few times with the same result Intravenous injection of ¼ mg of strophanthin daily had the same effect (Hauser and Scherf)

Coagulation of Blood In therapeutic doses digitalis was said to alter the coagulability of the blood With no change in the prothrombin time coagulation time was shortened (Massie et al) The frequent occurrence of venous thrombosis in cardiac cases has been ascribed to this effect of digitalis This effect of digitalis on the coagulation time has been denied recently (Sokoloff and Ferrer) but fast energetic digitalization is still said to increase the incidence of thromboembolism (Cormsen)

Extrasystoles Experimentally cardiac irregularities appear in cats after 75 per cent of the fatal dose of digitoxin and 60 per cent of the fatal dose of ouabaine are given This includes conduction disturbances (Krueger and Unna)

A very important sign of so called digitalis intoxication is the appearance of extrasystoles They are usually found as bigeminy that is every normal beat is followed by an extrasystole We put intoxication in quotation marks because healthy mammalian hearts do not develop the regular digitalis bigeminy even when treated with toxic doses It was not possible to observe this disturbance

of rhythm in man following the administration of toxic doses (suicides) or in animal experiments as long as the heart was in good condition Only the dying heart may show bigeminal groups in the very last minutes before standstill Extrasystoles like those observed in the cardiac patient which may persist for weeks are obtained experimentally however if the myocardium is chemically or mechanically damaged (Kobacker and Scherf) In a similar way digitalis causes extrasystoles in patients only if myocardial damage coexists The nature of this myocardial damage the necessary prerequisite was unknown until recently If extrasystoles develop during digitalis therapy in a cardiac patient it indicates that the heart muscle is abnormal Accordingly the prognosis is always dubious

Recent investigations show that a diminished amount of potassium in the heart muscle cells is responsible Skeletal and heart muscle lose some potassium when fatigued Toxic doses of digitalis have the same effect whether the therapeutic doses do so is not certain but possible The potassium content of the heart muscle was found diminished particularly in mitral lesions with chronic heart failure (Calhoun et al) it is usually in these hearts that digitalis bigeminy appears Lown could elicit digitalis extrasystoles when potassium was removed from the serum by hemodialysis and Page could precipitate ventricular arrhythmias in 7 of 37 digitalized patients by reducing the potassium level in the serum through the administration of carbohydrates Anoxia acidosis adrenalin insulin and glucose injections increase the potassium deficit in the heart Since it is not only the amount of digitalis but also the state of the heart muscle that is important for the development of these extrasystoles the term sign of intoxication in the usual sense is not entirely justified Some patients do not develop digitalis extrasystoles even if they take 0 2 Gm of standardized leaf daily for years while others develop them regularly after the third tablet of 0 1 Gm digitalis (personal observations) Five to seven grams of potassium chloride daily in fruit juice abolish these extrasystoles

Extrasystoles and bigeminal rhythm may occur in cardiac patients independent of digitalis treatment In these cases digitalis therapy — if indicated — is permissible and one will usually find that the extrasystoles disappear during the treatment In patients who show extrasystoles in the course of digitalis therapy however great caution should be observed before further doses of the remedy are administered If the treatment is continued in the presence of extrasystoles caused by digitalis the number of extrasystoles often increases resulting in the development of threatening tachycardias and even ventricular fibrillation If digitalis treatment seems necessary one may continue the treatment with small doses i e not more than 0 15 Gm daily The patient must be examined at least twice daily and the treatment must be discontinued if the number of extrasystoles increases Most — if not all — deaths due to the administration of digitalis are caused by the neglect of this rule In an advanced stage digitalis extrasystoles occur so irregularly and so rapidly that an anarchie ventriculaire appears (Mahaim) the examining physician is convinced that

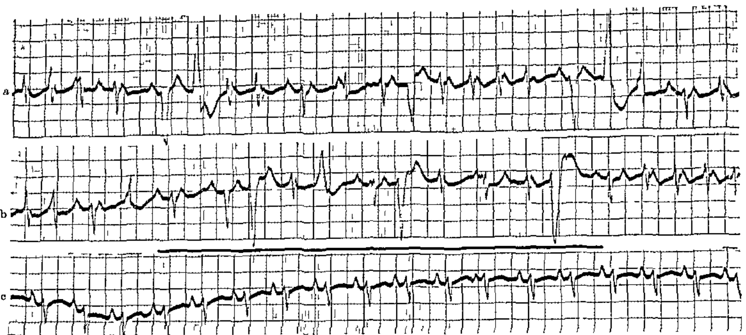


Fig 116 The top tracing (lead II) shows an atrial ectopic tachycardia and partial A V block in a 70 year old woman who had received 1 mg of digitoxin as a single dose Ventricular extrasystoles are also present In (b) the tachycardia remains during carotid pressure (the horizontal black line indicates the duration of pressure) it persists when pressure is discontinued Figure 116c shows a regular sinus rhythm interrupted by a single atrial extrasystole *11 days after the digitalis* had been stopped and after the administration of potassium



FIG 117

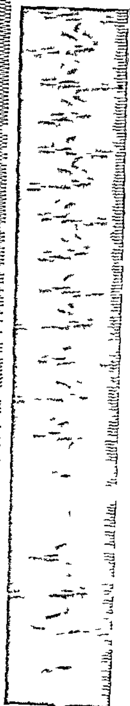


FIG 118

FIG 117 Atrial fibrillation and multiform ventricular extrasystoles with abnormal idioventricular ectopic beats caused by digitalis

FIG 118 Ventricular tachycardia with alternating form of ventricular complexes caused by digitalis There is also atrial fibrillation

he is dealing with atrial fibrillation and rapid ventricular action he increases the dose of digitalis and ventricular fibrillation is induced The principal reason that *the treatment with full therapeutic doses* — the administration of large amounts of digitalis in one or two doses — *should be completely abandoned* is that one can never predict after what dose of digitalis extrasystoles will appear Since they may develop even after a few *tablets* the administration of large initial doses may lead to dangerous and even lethal arrhythmias It is therefore understandable that most publications dealing with dangerous digitalis arrhythmias appeared when treatment with full doses was in vogue about forty years ago and again in recent years

Digitalis extrasystoles usually originate in the ventricles Reports of atrial extrasystoles caused by digitalis are scarce We have rarely seen them In all probability the reason for this rarity lies in the fact that the atria are under the influence of the increased inhibitory vagal tonus during digitalis therapy and this influence is lacking in the ventricles Experimentally the direct application of digitalis (or strophanthin) to the myocardium leads to atrial as well as to ventricular extrasystoles

Paroxysmal atrial tachycardias with partial A V block appear during the administration of

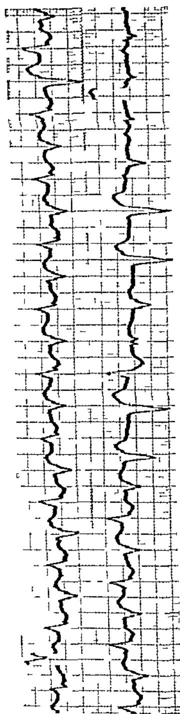


FIG 119 Ventricular tachycardia with alternating forms of the ventricular complexes in a patient with sinus rhythm The patient died suddenly presumably from ventricular fibrillation a few hours after the record had been registered

digitalis and disappear promptly after the exhibition of potassium chloride or acetate (figure 116)

The electrocardiogram usually permits the differentiation between digitalis extra systoles and the harmless ventricular extrasystoles that occur in the healthy The extrasystoles found so often in the healthy always originate in the same focus and show the same ventricular elec trocardiographic complex even if they persist for years Extrasystoles due to digitalis show a continuous variation of form since they originate in different foci and are due to an abnormal intraventric ular conduction (Scherf 1927) Extra systoles caused by organic heart disease (coronary sclerosis diphtheria) may also show varying forms of the ventricular complexes

This initiation of ectopic impulses by digitalis is a specific quality of the drug and is not caused by increased excitabil ity the latter is actually diminished

Figure 117 shows the electrocardio gram in the third lead of a patient with a rheumatic mitral lesion and extra systoles due to digitalis There is atrial fibrillation The first ventricular com plex conducted from the atrium in the tracing is followed by three multiform ventricular extrasystoles the second by one The third conducted complex is fol lowed by six extrasystoles and then by an abnormal automatic beat which is a characteristic digitalis effect

In figure 118 obtained from an other patient atrial fibrillation is also present (lead II) The first beat is fol lowed by three ventricular extrasystoles of different form The next beat after a pause is followed by a paroxysmal ventricular tachycardia with alternating form of the ventricular beats These

tachycardias precede the stage of ventricular fibrillation They are rarely seen except when digitalis is used in advanced myocardial damage They appear typically however if digitalis therapy is continued in cases of digitalis bigeminy

The important phenomenon of redigitalization is discussed in the next section

Elderly patients tend to show untoward effects after administration of moderate doses more often than younger individuals (fig 119)

Do age

It is not advisable to follow a fixed scheme of treatment The digitalization of every new patient represents an experiment with an unknown outcome One can never know in advance how much digitalis a patient will need Only after it is determined how the patient responds to treatment how much digitalis i needed to obtain a desired effect and how long it takes until compensation is restored should an opinion about the prognosis of a decompensated case be offered

Full Dose Treatment As was previously mentioned and for the reason just cited the practice formerly in vogue and recently reintroduced of treating every decompensated cardiac patient for a certain number of days always with the same amount of digitalis is not correct It is just as improper to give schematically an amount of digitalis calculated according to body weight This is done by pharmacologists in animal experiments but is not permissible in the sick patient whose reaction to digitalis treatment is unpredictable

In recent years a similar method the full dose therapy was recommended Without regard to weight age or degree of failure the dose of 1 2 mg of digitoxin is given at one time Others recommended 1 7 or even 2 2 mg is the full do e The statement that 1 2 mg of digitoxin may be given at one time with complete safety (Gold et al) is certainly wrong as many publications show On the other hand Evans et al give 2 mg of digitoxin to one patient without even obtaining a slowing of the rate

Four facts speak against this procedure In the first place patients with the same type of heart lesion of the same age and the same body weight and even the same degree of decompensation may require entirely different amounts of digitalis Furthermore the wisdom of administering large doses to restore compensation as quickly as possible may be doubted Naturally one wishes to help as soon as possible and to improve the cardiac condition in an emergency Nevertheless the average cardiac patient who requires digitalis for rapid ventricular action caused by atrial fibrillation or for decompensation does not have to be digitalized within 24 hours The old mechanical conception of decompensation no longer suffices We have learned that most tissues and cells of the body live under abnormal conditions in a patient with congestive heart failure the advantage of changing the situation quickly is questionable Nothing is gained by restoring the circulation in these patients within a few hours instead of a few days indeed the disadvantages are great The third and most important reason for

not utilizing the full dose treatment was mentioned in the preceding pages when it was pointed out that the appearance of dangerous extrasystolic arrhythmias even after small doses of digitalis can never be foreseen Finally caution against the employment of large doses is required because focal necrosis appears in the myocardium in the experimental animal after the administration of sublethal doses of digitalis While similar changes have not been observed in man even after the use of large therapeutic doses one should not forget that injury to the tissue cells may occur despite the fact that such injury may not be demonstrable by our rather crude histologic methods

Actually severe signs of intoxication have been seen particularly in elderly patients even after the administration of 0 6 mg of digitoxin (Fremont and King) We have seen toxic prefibrillatory arrhythmias and atrial tachycardias after 0 3 mg of digitoxin daily and the lassitude and nausea may persist for weeks

Not only does every species of animals have a different sensitivity to digitalis but the sensitivity of different members of the same species of healthy laboratory animals varies This is true much more for sick human beings who at different times need different doses

Furthermore a half dose in a patient with atrial fibrillation brings the rate down from 160 to 85 while the full dose brings the rate down from 160 to 75 in the same patient (Kay) The dangers of larger doses are infinitely greater The benefit is small

There is no average initial or maintenance dose except that which is calculated on paper Therapy is highly individual Therefore the recent revival of the full digitalizing dose assuming that the amount needed by every individual is the same independent of weight age etc cannot be accepted

Initial Dosage While treatment with excessively large doses of digitalis given within a short time should be avoided the administration of moderate doses proportionate to the severity of the decompensation is proper

One tenth of 1 Gm of the standardized (assayed) powdered leaves in the form of tablets will be considered as a standard unit Even here the strength may change Thus the assayed digitalis of USP XI was much stronger than that of USP X while the digitalis of USP XII was again slightly weaker

The dose given to a patient with mild decompensation who does not present severe manifestations of congestion may amount to 0 15—0 2 Gm a day of assayed digitalis in the form of powdered leaves or tablets In more severe cases of decompensation the daily dose is increased to 0 1 Gm three or four times daily

Only those subjects who are known to require much larger doses of digitalis than the average patient should receive about 0 6 Gm of digitalis daily This group comprises patients with hyperthyroidism fever or pulmonary embolism The literature on the question of the greater resistance to digitalis of patients belonging to one of these groups is large and somewhat contradictory It seems established however that slowing the heart in patients with hyperthyroidism combined with atrial fibrillation is difficult Why a larger amount of digitalis needed by virtue of the presence of fever is not yet decided Another une

difficulty in obtaining the desired slowing of the heart in atrial fibrillation is encountered in patients with pulmonaray embolism This complication should always be suspected if — in the absence of fever or hyperthyroidism — the expected effect of digitalis is not obtained

Large doses of digitalis are given only as long as evidence of severe decompensation persists As soon as improvement appears treatment is continued with smaller doses

One can never predict the duration of digitalis therapy Many days or even weeks may elapse before it appears that the best possible result has been obtained or until digitalis vomiting or bigeminy prevents further administration of the drug Long duration of the period of digitalis medication in itself is no contraindication for continuation of the treatment

Maintenance Treatment If digitalis therapy in a decompensated lesion or myocardial disease is carried to the point where the patient seems fully compensated and all signs of congestion have disappeared or when this result is impossible if the optimal state seems to exist the administration of digitalis should not be discontinued to be resumed only when the manifestations of decompensation reappear It is also improper to recommend a certain amount of digitalis purely schematically for a number of days each month for all patients It is better practice with most patients not to pause entirely in the administration of the drug an adequate amount should be given to maintain the patient in the best condition attainable by treatment

In cases of atrial fibrillation in which digitalis is given only to keep the ventricular rate low the rate itself is the best guide for the dosage These cases in particular require maintenance treatment Patients who develop decompensation following an acute infection or excessive physical effort may not require maintenance treatment Full compensation may be preserved if the cause for the decompensation has vanished

The dose for maintenance treatment should also vary according to the needs of the patient If compensation was readily restored and if this was achieved with relatively small doses of digitalis 0 1 Gm digitalis given once on every day or on every second day may suffice If larger doses were originally required for a long period the maintenance doses also will usually be larger One will find that some patients may need 0 2 or even 0 3 Gm of digitalis every day because even a temporary and slight reduction of the dose causes the reappearance of signs of decompensation Naturally the amount of digitalis required by the individual patient will not always be found instantly after some observation the doses may have to be increased or decreased Likewise the unavoidable alteration of the sensitivity of the patient changes of the heart and also changes of the strength of the drug may force a change of dosage Digitalis made by different manufacturers which were assayed cause quite different responses in man at different times and in addition the absorption and stability of different preparations varies

For these reasons patients who require maintenance treatment with digitalis need periodic re examination by their physicians By the continuous adminis

tration of digitalis patients avoid the frequent change from compensation to decompensation and within certain limits they may be kept active for years There is no danger of acquiring tolerance for digitalis from prolonged administration the drug always remains effective

If some untoward sign mentioned in a previous chapter including digitalis extrasystoles appears and one finds that continued treatment is necessary merely diminishing the dose often will suffice If the patient does not tolerate even the smallest doses without exhibiting side effects one may be compelled to stop the drug completely and try again after a short period during which other cardiac stimulants such as caffeine or theophylline are given

Different Preparations of Digitalis

In selecting a preparation it should be remembered that the galenic forms of digitalis are still among the most reliable provided the assayed drug is employed

The powdered leaf or the tablet made from powdered leaves are most commonly used Formerly digitalis tincture was used widely if fresh it is very satisfactory It is rarely prescribed at present and perhaps should be avoided because it must be fresh and reliable in order to give good results The deterioration of tablets or powdered leaves by storage is negligible

The number of special digitalis preparations on the market is legion and new ones constantly appear Most of these preparations are satisfactory Few have any advantage in comparison to assayed digitalis tablets If a new preparation is tried the physician should familiarize himself with the correct dosage which is frequently at variance with the manufacturer s recommendation Only experience gained by the use of the preparation in many patients will show its value It is unwise for the physician to change continually to new and different preparations and to adopt at once those which are highly eulogized Certain advantages are claimed for every new preparation of digitalis Many of these attributes to be sure are based on experimental investigations on the frog or cat heart and have little value at the bedside If it is asserted that a preparation is nontoxic does not cumulate and does not produce vomiting it should not be employed it is inert A good preparation of digitalis is toxic does cumulate at least to a slight degree and must cause vomiting when it is administered in sufficiently large doses

Preparations of digitalis made from the whole drug (Digifortis Digalen Digilanid Digifolin and many others) contain a mixture of glycosides and possess no advantage over the standardized preparations they are rarely used in the United States today They may be used where the standardized powder or tablets are unobtainable The physician is advised to employ only one or two of these preparations in order to obtain some experience Even the strength of these special preparations may change for various reasons and a physician who does not thoroughly know the digitalis employed may become aware of this change too late It is a great handicap to work with two unknowns the preparation of digitalis *and* the patient

Most good commercial preparations are assayed One should not rely however too strongly upon the statement of the manufacturer for dosage The amount should be determined on the basis of personal experience If the directions printed on packages are followed the dose prescribed frequently is too small

Every physician should be acquainted with the action of a few special preparations of digitalis Some are very powerful Since some are obtainable in the purified crystalline state the dosage is exact and the biologic assay with all its difficulties is unnecessary

The oldest pure crystalline digitalis glycoside is digitoxin (digitaline Nativelle) It is quantitatively absorbed when given orally The different preparations of digitoxin are not of equal purity and not of equal strength A dose of 0 1 mg given three times daily is as active as three tablets of 0 1 Gm powdered leaves given daily Only for special purposes e g to transform atrial flutter into fibrillation should larger doses be given and then only under close supervision Nausea and vomiting soon appear with large doses Digitoxin is fixed to the albumin fraction in the blood and disappears completely from the blood only after 24 hours It is therefore not one of the rapidly acting glycosides Only 7 per cent of the glycoside is dissipated daily in the heart muscle Therefore digitoxin is a glycoside with a great tendency to cumulate For the restoration of compensation in patients with coronary sclerosis or following a myocardial infarction preparations of digitoxin are very useful In many patients the prolonged administration of 0 2 mg daily is necessary to preserve compensation In others particularly in elderly people this dose is too large and causes toxic phenomena to appear Some patients need 0 1 mg every other day or even smaller amounts

A very satisfactory glycoside isolated from digitalis lanata is the crystallized digoxin (Smith) It can be given by mouth or by injection Following an intravenous injection ventricular slowing begins in five to ten minutes and the maximum effect is attained within an hour After oral administration improvement begins within an hour and may be pronounced within six to seven hours Tablets contain 0 25 mg of digoxin and the material for injection contains 0 5 mg per ml

The third crystalline glycoside also isolated from digitalis lanata is Cedilanid (lanatosid C) The components originally isolated (digilanides) were found to cumulate less than digitoxin Ampules and tablets are available One ml of the liquid contains 0 2 mg of Cedilanid The first dose is usually 2—4 ml It may be repeated on the next day according to the condition of the patient

Lanatosid C is bound but little to blood proteins and acts quickly almost like strophanthin It is rapidly eliminated

Acetyl digitoxin is also derived from the digitalis lanata It is obtained from lanatosid A fraction by enzymatic cleavage of 1 molecule of glucose It is absorbed rapidly Therefore it is recommended particularly for paroxysmal tachycardias and fibrillation (Loeffler et al)

Citalin a mixture of amorphous digitalis glycosides that has been employed on the European continent for many years recently has been reintroduced (Batter

man) We employed it for many years as Verodigen and found it reliable However the claim that gitalin (amorphous) helps when other glycosides fail is unjustified

Method of Administration

In the majority of cases digitalis is given by mouth in the form of the assayed powder tablets drops or pills of one of the reliable commercial preparations In exceptional cases in which more rapid effects seem necessary digitalis is given intravenously using a crystallized pure glycoside (digitoxin digoxin cedilanid)

The rectal suppository represents another method of administration but it is rarely used in this country By rectal administration of purified digitalis gastric irritation due to ballast substances and saponins is avoided Furthermore the drug is absorbed by the mucosa and conducted by the hemorrhoidal veins into the inferior vena cava without retention in the liver The rectal administration of digitalis has the same effect as a slow intravenous infusion The amount of digitalis which should be given by rectum is the same as that which would be given by mouth

It is easy to administer the whole dose of digitalis for the day in the form of two suppositories in this way one obtains better absorption without gastric irritation Particularly in those patients who present evidence of marked hepatic congestion or who for some reason are unable to receive injections of a crystalline digitalis glycoside or strophanthin suppositories are useful

One of the best is the digilanid suppository If a dose or a preparation different than that obtainable from the manufacturer is desired the suppositories can be prepared by any pharmacist by mixing the corresponding amount of a purified digitalis preparation (digitaline digalen digilanid) with cacao butter Usually it is possible to mix about 15 drops of an appropriate digitalis solution in the amount of cacao butter required for one suppository

Another advantage of a suppository is the possibility of admixing other substances which must be administered by rectum Thus patients with Cheyne Stokes breathing may need aminophylline in addition and if necessary an hypnotic may be added For example

Digalen	0 5 ml
Aminophylline (Theophylline ethylendiamine)	0 5 Gm
Ol Cacao q s f suppos	

One suppository may be given in the morning and sodium phenobarbital may be added to another which may be administered in the evening

It is not advisable to administer digitalis intramuscularly since local pain invariably follows and the temperature rises indicating muscular necrosis

Preparations with Digitalis Like Action

There is a large number of so called digitalis preparations of the second order they are powerful and active drugs Most of these preparations have effects similar to those of digitalis but rarely do they accomplish more than digitalis In the rare case of idiosyncrasy to digitalis such agents may be em

ployed we find them useful on patients who are under the impression that the administration of digitalis means the beginning of the end

Squill is perhaps the best known representative of this group It is at the same time one of the oldest known drugs being mentioned in the Ebers papyrus From the drug a pure crystallized glycoside, Scillaren A has been isolated (Stoll) and its activity can be compared with good preparations of digitalis The single dose of Scillaren by mouth is 0 8 mg the suppositories contain 1 mg of the glycoside The side effects if these drugs are employed are the same as those of digitalis including ventricular extrasystoles

Among the other drugs of this group (Adonis vernalis Nerium Antiaris Convallaria majalis) only Helleborus deserves mention Its purified extracts proved very active in its pharmacologic characteristics it stands midway between digitalis and strophanthin (Scherf)

STROPHANTHIN

Closely allied to the digitalis glycosides although different in many respects are the glycosides of strophanthus Of the many compounds in this group only three are used clinically

Preparations

K Strophanthin Strophanthin kombè or k strophanthin is an amorphous powder In recent years it has been possible to isolate a crystalline glycoside from k strophanthin which represents about three quarters of the amorphous glycoside It is called strophoside K strophanthin is mentioned in the United States and in the British Pharmacopoeia and it was widely used in Germany under the leadership of Fraenkel

G Strophanthin Strophanthin gratus or g strophanthin was isolated as a more stable crystalline product by Arnaud (1888) and is called by its African name ouabain This preparation is widely used in French medicine

Acetyl strophantidine an aglucone is a synthetic preparation prepared from the seeds of strophanthus kombe It works more rapidly than any other preparation and therein lies its danger Toxic rhythms are common and in our opinion there is no place for the use of this compound in clinical medicine

Pharmacologic Effects

The action and side effects of strophanthins on the heart muscle particularly on systole and on the blood vessels are identical to those of digitalis Some of the differences are their great solubility in water the small amount of fixation of strophanthin in the heart and — in connection with this — the slight cumulation If a dose of digitoxin is given 93 per cent of the drug is still present in the heart after 24 hours and 50 per cent after 9 days Of a dose of lanatoside C after 24 hours only 80 per cent is present and only 64 per cent after 48 hours Of strophanthin only 50 per cent of its action is present after one day and only

one eighth after three days (Rothlin and Bircher) The most important difference from a clinical standpoint has been the almost immediate action of strophanthin This is advantageous when it is necessary to improve a severe decompensation rapidly With the pure crystalline glycosides of digitalis purpurea (digitoxin) and digitalis lanata (digoxin cedilanid) which may be given intravenously only slightly less rapid action (30—60 minutes) is obtainable

There are few potent drugs about which opinions are as divided as strophan thin (Kisch) While in some countries particularly on the European continent strophanthin is employed in practically all types of decompensation much more often than digitalis and in many large institutions seems to be the drug of choice in other countries strophanthin is scarcely known

Several facts account for this difference of opinion First overenthusiastic physicians stressed the digitalis like effect of strophanthin and went so far as to use it as a synonym for digitalis neglecting however to stress the important and essential differences between the two Second the doses recommended (even in recent times) were much too large led to untoward effects and discouraged the physician from further use Third most preparations of strophanthin are quickly destroyed particularly by the alkaline glass of the ampules and lose their potency within a short time Therefore many preparations now dispensed are disappoint ingly weak unless certain types of glass are used for the containers If injection of the inactive contents of these ampules a few times in emergencies elicits no effect the disappointed physician doubts the reports of other observers and decides to use only digitalis in the future

The ampules of ouabain at present are the best preparation of strophanthin obtainable in this country

Indications

In general strophanthin is indicated in the same conditions as digitalis Since these preparations are active only if given by injection there is the disadvantage of greater expense to the patient for he is forced to have an injection daily or almost daily for some time accordingly we feel that for routine treatment digi talis is by far preferable and that strophanthin should be given only on definite indications

Formerly the fact that its exact dosage could be prescribed without the necessity of bioassay was of great advantage but such procedure is also possible now with the crystalline preparations of digitalis

Strophanthin is indicated in an acute emergency If for example in an untreated or inadequately treated pregnant woman with mitral stenosis acute heart failure appears during childbirth or if a protracted and severe pulmonary edema appears in a patient with hypertension and does not react well to sympto matic therapy or if a patient is admitted to the hospital with a surgical emer gency requiring immediate operation and atrial fibrillation with a very rapid ventricular rate is found the administration of strophanthin will usually bring noticable improvement within a few minutes However it must be stressed

is present due to pulmonary congestion In these cases rapid dehydration may furnish quick relief In the majority of cases however treatment with diuretics is initiated only after the circulation has been improved somewhat by digitalis Often even the strongest diuretics evoke only a slight response when given to congested and decompensated patients If diuretic treatment is delayed a few days until the circulation is improved somewhat by digitalis striking effects may be obtained with much smaller amounts of diuretics Often the diuretics even become superfluous because rest in bed diet and digitalis alone cause a profuse diuresis

The *diuretics which are the most effective and if properly employed* distress the patient least by unpleasant untoward actions particularly on the gastrointestinal tract are certain organic preparations of mercury Since their use is not permissible in some cases every physician should be acquainted with the xanthine derivatives and other diuretics as well The action and the method of administration of the latter preparations will be considered first

Xanthine Derivatives

Xanthine preparations (purine bodies) have caffeine theobromine and theophylline as chief representatives While caffeine exerts its strongest effect as a stimulant of the central nervous system theobromine and theophylline are pronounced diuretic agents They also dilate the coronary arteries

All these preparations increase water and sodium chloride diuresis This effect seems to be accomplished by a direct action on the kidney Diminished tubular absorption has been assumed partly it is due to improved contractility of the heart and to mobilization of water and salt in the tissues Vasodilatation and better perfusion of the kidney originally held responsible seem to play a minor role All these drugs also stimulate the heart Thus theophylline increases the output of the damaged heart of the dog in the Starling preparation This effect is independent of changes of the coronary blood flow

Caffeine is rarely used as a diuretic since its stimulating action on the central nervous system is so pronounced that it leads to unpleasant sensations

The xanthine preparations most commonly used as diuretics are theobromine and its salts or *theophylline with various combinations*

The customary method of administering moderate doses of xanthine bodies distributed throughout the day often produced little diuretic action It is better not to scatter the doses rather large amounts should be used at short intervals and only for a short time

If the diuretic effect of one of these drugs ceases there is no justification for continuing the remedy with larger doses It is better to prescribe another preparation which may act excellently although it may be closely related to that which was originally given

Pure Theobromine In using pure theobromine we observed the best effect when it was given in [illegible] after lunch and if the same dose was repeated

two and four hours later thus a total of 3 Gm are given in divided doses in the afternoon If patients become too stimulated by the drug and sleep is disturbed theobromine may be administered after breakfast and two as well as four hours later

Theobromine Calcium Salicylate This drug known under the name Theocalcin is said to cause less gastrointestinal disturbance but we found no difference in comparison to some of the other purine bodies The dose is 3 Gm daily

Theophylline The strongest diuretic effect is obtained with pure theophylline It is best to administer it in enteric coated tablets similar tablets are also available for some of the other xanthine preparations The diuretic effect of theophyllinum purum is much stronger than that of theophylline with ethylendiamine (amin ophyllin euphylline) or theophylline with sodium acetate The rule of giving large doses within a relatively short time is particularly applicable with this preparation The best diuretic effect is obtained if 0 3 Gm is given after meals three times a day but only on every fourth day Such jolts of theophylline are greatly superior to small doses daily The 24 hour diuresis may amount to 5 liters Sometimes pure theophylline given in this way may be effective when mercurial diuretics fail (Faltitschek and Scherf)

If the preparation is used in the same dosage daily its diuretic effect often ceases completely within a few days If administered only on every fourth day as is the case with the mercurial diuretics it remains active for an indefinite period

Vogl recommends 0 5 Gm of aminophyllin injected intravenously twice daily very slowly for the purpose of diuresis

Untoward Effects Whenever xanthine preparations are administered it is well to inform the patient that untoward effects may occur In the event that such phenomena appear the patient is not taken by surprise and is not alarmed Moreover he is informed in advance that discontinuance of the remedy will afford rapid relief If the patient is unacquainted with the possibility of unpleasant untoward reactions the appearance of nausea vomiting severe headache and restlessness with increased excitability may be alarming All these phenomena are more common with theophylline than with other xanthines To counteract the central stimulating effect the administration of phenobarbital (0 03—0 05 Gm) with each dose of theophylline is recommended

A rare but nevertheless important contraindication to theophylline is epilepsy The preparation stimulates the cerebral cortex and may lead to attacks in epileptic individuals This effect as well as headache and hyperirritability are also prevent ed or diminished by the addition of phenobarbital to each dose of theophylline

Antidiuretic Action of Sedatives Analgesics and Hypnotics

Phenobarbital in the doses mentioned does not depress the diuretic action of theophylline Larger doses however as well as moderate doses of morphine or aminopyrine may not only abolish the effect of diuretics but may also inhibit normal diuresis to a high degree

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Pure Theobromine In using pure theobromine we observed the best effect when it was given in doses of 1 Gm after lunch and if the same dose was repeated

The administration of potassium salts as diuretics has been revived in recent years Potassium chloride or acetate are recommended Doses of about 5 Gm daily seem to be optimal Potassium chloride is obtainable in enteric coated tablets Occasionally nausea occurs during the administration of the drug and methemoglobinemia has followed the use of potassium nitrate If large doses are used or if kidney function is impaired the level of blood potassium increases The acid base balance is changed in some patients toward the acid side

Mercurial Diuretics

Type of Preparations Some inorganic mercurial preparations e g calomel have been used for many years as diuretics The action of calomel however was unreliable and intoxications were frequent The discovery of the diuretic action of organic soluble salts of mercury in 1920 was one of the greatest advances in the treatment of cardiac patients in recent years The duration of life in many patients is prolonged for years and countless others are enabled to lead an active life with the employment of these drugs The discovery was quite accidental Novasurol (Merbaphen) was used for about three years in the treatment of syphilis until its diuretic action was observed in a case of syphilitic aortitis (Saxl and Heilig Vogl) Later Salygran (mersalyl) and novurit (Mercupurine Mercurin) were introduced as well as neptal esidrone Mercuhydrin Thiomerin and others It is often claimed that the first preparation Novasurol (Merbaphen) was more toxic than the others but it seems that as experience increased the preparations were used more cautiously and therefore toxic manifestations became rare These diuretics contain about 40 mg of mercury per ml

Since the introduction of Mercupurine (novurit) which contains a very small amount of theophylline it has been claimed that this addition considerably enhances the diuretic effect of the mercurial salts Therefore theophylline was also added to most of the other preparations It is claimed that the addition of theophylline makes the mercurial diuretic less toxic and that they are less irritating locally when injected intramuscularly At bedside in appropriate cases by alternating the use of mercurial diuretics with and without theophylline we were unable to discover an appreciable difference

Fundamentally the diuretic action of all above named mercurial preparations is equal It has been claimed however that some such as neptal and esidrone are slightly more toxic than the others Mercupurine seems to act a little sooner and diuresis follows the injection more rapidly But the end result is the same as with the other diuretics The remarks which follow are equally applicable for all preparations including Mercuhydrin and Thiomerin which is a mercaptan compound and which can be given subcutaneously

Pharmacology The preparations lead to a marked water diuresis and to a relative and absolute increase of the sodium chloride diuresis More than 40 Gm of sodium chloride may be excreted in 24 hours In a boy of 16 years 1 ml of neptal caused a diuresis of 14 430 ml of urine in 24 hours 570 ml of urine were

in the urine of patients with congestive heart failure is increased The presence of a concentrated dark urine (after exposure to air for a few hours) due to urobilin shows that it is safe to use mercurial diuretics

The presence of colitis in any form constitutes another contraindication to mercurials Colitis is one of the most dangerous manifestations of mercury intoxication and therefore the administration of these compounds should be avoided when colitis is already present It is also unwise to give purgatives which irritate the large intestine on the days of the injection of mercurial diuretics Decayed neglected teeth and the presence of a profound anemia or cachexia are further contraindications since mercurial diuretics have a relatively high content of mercury and therefore act as cell poisons

Untoward Effects Mercurial diuretics may cause untoward effects by different mechanisms those of mercury intoxication those due to hypersensitivity or those caused by a too marked loss of water and electrolytes

MERCURIALISM The earliest indications of mercury intoxication are metallic taste salivation gingivitis stomatitis and colitis The latter is often hemorrhagic in character The patient may collapse so suddenly that no melena occurs All these manifestations of mercurial intoxication were rare since the preparations were used with proper caution and in appropriate cases Unfortunately it has been recommended recently that mercurial diuretics be given in intervals that prove to be too short with the result that evidence of intoxication is observed more often Agranulocytosis may occur

To counteract the effect of mercury BAL (5 mg per Kg) is given intravenously every 4 hours

HYPERSENSITIVITY Hypersensitivity to the mercury ion may exist but more often it is connected with the specific organic compound used Therefore change of the preparations often helps to avoid further abnormal reactions Dizziness fall of blood pressure drowsiness and headaches urticaria and erythematous dermatitis may appear fever collapse and cyanosis with death in a few minutes have been observed Dyspnea and attacks of asthma have followed even the first injection There is experimental and clinical evidence that ventricular extrasystoles paroxysmal tachycardias and ventricular fibrillation may appear owing to the direct effect of the mercury ion on the heart muscle These effects particularly the cardiac arrhythmias appear for the most part after intravenous injections

CONSEQUENCES OF DIURESIS The loss of water sodium and chloride causes somnolence cramps in the calf muscles and sometimes delirium or mental confusion Profound weakness may appear due to loss of potassium Therefore fruit juices should be ordered These complaints were known to follow a profuse diuresis long before the mercurial diuretics were introduced Since the excretion of sodium and chlorides need not parallel the water diuresis occasionally one observes these phenomena after moderate diuresis but may miss them after an unusually profuse one

The loss of calcium ions may lead to tetany Acute gout has appeared in a series of patients who had had previous attacks of gout A disturbance of electrolyte balance may be responsible

It has been claimed that the influx of fluid from the tissues increases the coagulability of the blood and therefore increases the danger of thrombosis and embolism

Fever and cutaneous manifestations (rash) may develop after an injection The fever may reach 39 C but rarely lasts longer than 24 hours the simultaneous use of calcium gluconate may help avoid these complications

However the intravenous injection of calcium preparations is dangerous especially in digitalized patients In one personally observed case it was followed by ventricular fibrillation in another patient who had not received digitalis before a long and dangerous ventricular standstill instantaneously followed the injection Intramuscular injections of calcium salts are free from these dangers

The appearance of abnormal reactions cannot be predicted They have been observed in patients who responded normally to preceding injections If however an abnormal reaction occurs once it is unwise to employ the intravenous route Sudden lethal accidents are not observed after intramuscular injections of mercury

While collapse or even sudden death immediately following an injection due to allergy undoubtedly occurs such catastrophes are rare and should not militate against use of these excellent agents Several series of more than 8000 injections have been reported without the occurrence of any untoward effect

The profuse diuresis may lead to an acute urinary retention in elderly patients with prostatic hypertrophy

Two other side effects of therapy with mercurial diuretics merit attention

(1) THE LOW SALT SYNDROME This develops in patients who receive mercurial diuretics too often while on a salt free diet or when losing much salt from the kidney The diuresis in these patients stops and they gain in weight they have low plasma levels of sodium (from 140 to 120 mEq per liter or less) and chlorides (from 100 to 86 mEq per liter or less) drowsiness and weakness may appear simultaneously Nausea and vomiting may occur and abdominal cramps are common There is a low carbon dioxide combining power and the urea as well as the NPN are increased often to values over 100 This acidosis and azotemia are rarely relieved by the infusion of hypertonic saline solutions (200—300 ml of a 5 per cent sodium chloride solution) since irreversible intracellular changes appear The outcome is usually fatal The syndrome occasionally appears in cardiacs without ascertainable reason (movement of electrolytes? abnormal water retention? action of aldosterone?)

(2) HYPOCHLOREMIC ALKALOSIS (low chloride syndrome) The excretion of chloride under the influence of an injection of mercury is excessive and may be greater than that of sodium When the chlorides fall below 86 mEq per liter no diuresis results from the injection A fall by only 4—6 mEq may be of

Ammonium chloride is necessary only if mercury alone does not suffice or if injections of mercury are repeated at short intervals and the danger of hypochloremia exists

If doses not larger than 2 ml are given intramuscularly at intervals of no less than four days *no accident will be seen in the course of many thousands* of injections apart from hypersensitivity Certainly the injections must be discontinued at once with evidence of colon irritation or stomatitis It is astonishing how well the injections are tolerated One of our patients received more than 700 injections in 14 years Such patients are often observed and receive their injections on every fourth or fifth day without any sign of renal irritation

The combination of a mercurial diuretic with decholin (5 ml) in the same syringe injected very slowly has been frequently recommended However unpleasant accidents caused by decholin have been observed

No examination gives us as clear a picture of the effect of our diuretic therapy as weighing the patient

Mode of Administration The customary method of administering mercurial diuretics was for many years by intravenous injection The injection must be properly performed Some patients are so sensitive that the small amount of the preparation on the needle to say nothing of a paravenous injection suffices to cause a severe necrosis of the skin that requires months to heal For this reason the needle through which the preparation is withdrawn from the ampule is never employed for the injection The preparations are injected only if one is absolutely sure that the injection is exclusively intravenous

Intramuscular injections are now the method of choice since dangerous hypersensitivity reactions can thus be avoided they usually do not hurt or are only slightly painful The original mercurial organic diuretic novasurol it may be recalled was for years given only intramuscularly none dared to essay intravenous injection Painful infiltration following intramuscular injection is avoided if 1 ml of a 1 per cent solution of procaine (or a similar preparation) is added to the mercurial preparation in the same syringe The addition of procaine not only prevents any immediate (though slight) pain but it prevents secondary inflammation and irritation (Freud and Meyer) The best site for the injection is located in the posterior axillary line three fingers below the crest of the ileum In obese patients the injection must be made with a needle of sufficient length if this precaution is not taken the injection may actually be subcutaneous or be made into the deep adipose tissue where it causes necrosis A true intramuscular injection never causes necrosis

All injections should be given early in the morning The diuresis follows the injection in two to three hours and for the most part is over by bedtime If the injection is given later during the day the night rest is disturbed The injection of mercurial diuretics into a pleural effusion or into ascitic fluid is dangerous and may lead to serious local irritation Marked diuresis may follow such injections but they possess no advantage The appearance of a profuse diuresis following an intra

peritoneal injection (done only in the presence of ascites) begins within a few hours and rarely exceeds two days This proves that ascitic fluid is quickly absorbed and reformed otherwise the rapid action of the injection would be incomprehensible

Suppositories of mercupurin or those made from some other organic mercurial diuretic produce a considerable diuretic effect (Dennig and Krause) They should be inserted after a cleansing enema The suppository should be covered with pantocaine or nupercaine ointment Fissures and hemorrhoids are a contraindication Since some suppositories contain a rather large amount of the active ingredient they should not be given more often than every four days Many times the suppositories cause diuresis only after preliminary preparation with ammonium chloride When the administration of injections is impossible for some reason suppositories may be tried

The oral administration of the organic mercurial diuretics was tried early (Saxl) and has been recommended repeatedly If 2 to 3 tablets are given daily some diuresis may be obtained Often evidence of intoxication develops and in one series of 39 cases toxic effects appeared in 14 This also holds for preparations introduced recently and declared nontoxic Orally administered mercury is often excreted days after its ingestion and cumulative effects are common

Ammonium chloride nitrate and sulfate if given in sufficient doses may alone provoke a moderate diuresis and increase the diuretic effect of the mercurials In the body the ammonium ions are synthetized to urea and the acid radical remains Ammonium chloride is preferred because methemoglobinemia has followed the employment of ammonium nitrate The mode of action is not entirely clear Presumably acidification may help to liberate mercury in the renal tubuli The administration of an acidifying diet also increases the water and sodium chloride diuresis caused by theocin (theophylline) A similar purpose is served by the administration of 20 ml of dilute hydrochloric acid in 500 ml of water

Large doses of ammonium chloride are recommended We advise 6 Gm ammonium chloride in enteric coated tablets (i e 6 tablets of 1 0 Gm) daily for two days before and 3 Gm on the day the injection is given Others suggest smaller doses for instance 2 Gm of ammonium chloride two hours before the mercurial diuretic is injected Untoward effects (gastric irritation) are rare with enteric coated tablets In many cases ammonium chloride is unnecessary since the mercurial injection alone affords a satisfactory result There is no justification for administering ammonium chloride daily for a long time prescribed in this manner it loses its diuretic action and causes acidosis

Diomax — Diuril

A mild diuretic effect of sulfonamides has been known for a long time and one synthetic preparation Diomax with a new organic structure (acetazoleamide) has a marked diuretic action with very few side effects

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the hydrogen cycle and 20 per cent in the potassium cycle Finally Katonium up to 75 per cent an ammonium and 25 per cent a potassium resin is given in doses of 15 grams three times daily

The resins also seem to absorb riboflavin and thiamin Since the absorption of potassium may lead to a dangerous hypokalemia one third of the resin is in the potassium cycle so that potassium ions are available for reabsorption Intake of resins can also cause hyperchloremic acidosis because hydrogen ions are released and basic ions lost in the feces chlorides are not removed by the usual resins Therefore a large percentage of the resins are in the ammonium cycle and are able to release the ammonium in the gastrointestinal tract

In vitro 1 gram of resin removes approximately 10 mEq of sodium but in vivo the amount depends upon the intake of sodium and on other factors

The acidosis is partly compensated by ammonia formation and the excretion of more carbon dioxide via the lungs The acid urine may cause albuminuria and casts to appear

While resins can be prescribed with reasonable safety they should never be administered in the home continuous control of the sodium chloride potassium blood levels as well as of NPN and carbon dioxide combining power are needed With the increase of chloride in the blood and a decrease of bicarbonate plasma concentration there is great danger of a high NPN Prolonged administration resulting in the removal of calcium may lead to bone demineralization With removal of potassium digitalis toxicity appears in patients taking this drug and dangerous arrhythmias occur Rarely fecal impaction occurs

Whenever loss of appetite weakness or vomiting appear therapy should be discontinued and one should check the blood for the substances mentioned above

The granulated resins are best taken with cream as in a cereal the powdered forms with orange or other fruit juices which also serve to supply potassium.

The indications are few While diet may be more liberal and may contain more salt few people like the resins which taste like sand and which they must ingest only in order to get more of the food they desire In patients who are sensitive to mercury that is to all mercurial diuretics the resins may save or prolong life It should be stressed however that even if resins are taken the diet can never be really liberal

Renal damage is an absolute contraindication Many refuse the resins because of diarrhea or constipation vomiting nausea or loss of appetite

Southey Tubes

When all diuretics fail and tense edema is present drainage with Southey tubes is necessary This represents a last resort since the danger of secondary infection and the development of erysipelas is great Fortunately this procedure has rarely been necessary since the introduction of the mercurial diuretics But there are times when tubes must be employed because all other therapy is fruitless

We have seen patients who responded to ordinary diuretics well only after the successful employment of the Southey tubes and then were kept free from edema for years

TREATMENT OF CHEYNE STOKES RESPIRATION

Cheyne Stokes breathing and the various forms of paroxysmal nocturnal dyspnea which result from cardiac failure (left ventricular failure) represent indications for digitalis therapy However some time elapses before digitalis helps unless the rapidly acting pure glycosides or strophanthin are given Furthermore not every patient is relieved by digitalis and signs of failure may persist despite energetic digitalization Therefore it is often necessary to treat Cheyne Stokes respiration symptomatically

Oxygen Since an oxygen deficit and hyposensitivity of the centers have long been recognized as precipitating causes of Cheyne Stokes breathing frequently an effort has been made to obtain improvement by means of oxygen inhalation as well as by agents which stimulate the cerebral centers

As a matter of fact the inhalation of oxygen acts immediately and abolishes Cheyne Stokes in most cases only a few patients do not respond The apneic pauses vanish and respiration becomes regular Naturally improvement persists only as long as the administration of oxygen is continued

Inhalation of oxygen by nasal catheters is useful and may tide the patient over distressing periods The great anxiety and restlessness of the patient with a severe form of Cheyne Stokes often interferes with their use and makes the employment of oxygen masks also impossible The oxygen tent is superior and may quickly abolish periodic breathing as well as the mental confusion and restlessness combined with it

Central Stimulants All attempts to influence Cheyne Stokes respiration by the administration of central nervous system stimulants have failed Lobeline strychnine atropine and coramine as well as caffeine are useless for this purpose

Aminophylline (Theophylline with ethylenediamine) which is also known as metaphylline euphylline has an almost specific action This compound was used for many years as a diuretic and vasodilator while its excellent effect on patients with Cheyne Stokes breathing was only occasionally mentioned until this action was stressed by Vogl The relief afforded by the preparation is so great that the term miraculous is often used by patients and even by the physician in charge

A few minutes following the injection the periodic alternation of dyspnea and apnea disappears and the respiration becomes regular With this the restlessness and anxiety subside and patients who have not had a good night for weeks sleep quietly It acts like magic The patient is not compelled to sit up nor to pace the room restlessly but lies quietly in bed seeming and feeling altogether like a different person

The most effective method of administering the preparation in patients with Cheyne Stokes is the intravenous injection An ampoule containing 0 24 Gm of aminophylline is injected very slowly A rapid injection leads to marked vaso

dilatation and flushing with the sensation of warmth not unlike the sensation following an intravenous injection of a calcium or quinine preparation In the patient suffering from a cardiovascular disorder too rapid an injection may be followed by vertigo marked fall of blood pressure and even a mild collapse Therefore the aminophylline should be diluted with saline or a 5 per cent solution of glucose and injected so slowly that the injection requires at least 5 minutes If this method is followed no harm need be feared It is best to give the injection during the evening since Cheyne Stokes respiration tends to occur or to become worse at night If necessary an injection can be given twice in 24 hours Hyper sensitivity to aminophylline (headache vomiting) is rare This treatment may be continued for a long time the mere fact that the preparation is employed over a considerable period is in itself no reason for stopping it

Intramuscular injections are not recommended because they often cause pain Occasionally however an intramuscular injection is well tolerated perhap due to a better balance of the hydrogen ion concentration The dose for intramuscular injections may be the same or a double amount (0 48 Gm) Almost as effective as an intravenous injection is a retention enema An ampoule containing 0 48 Gm or a corresponding amount of aminophylline powder (0 5 Gm) is diluted with about 30 ml of tap water and given as a retention enema Similar but a little less effective is the administration of aminophylline in a suppository containing 0 5 Gm The administration of aminophylline as a suppository results in satis factory levels of theophylline in the blood plasma (Glass et al) One suppository is given at bed time and another during the day if necessary Aminophylline tablets have little value in Cheyne Stokes breathing

The mode of action of aminophylline is still obscure Aminophylline is a vasodilator but this effect is hardly responsible for the improvement since stronger vasodilators like the nitrites and even large doses of nitroglycerin are not effec tive in Cheyne Stokes respiration Theophylline like all xanthine bodies is a central stimulant But other central stimulants even though stronger like caff eine do not influence Cheyne Stokes breathing We are dealing therefore with a specific effect of the preparation It has been maintained that other theophylline preparations for example theophylline with sodium acetate have no effect on periodic breathing while ethylene diamine and some other amines influence the breathing like aminophylline According to our observations however intra venous injections of theophylline sodium acetate act favorably on Cheyne Stokes respiration and we have seen equally good effects when urea was used as a solvent for the theophylline instead of ethylene diamine The explanation of the action of aminophylline in Cheyne Stokes is made more difficult by the recent discovery (Kety) that after injection of this compound the cerebral blood flow is decreased and not increased

Not rarely the patient reports in the morning after having had an evening dose of aminophylline that the night could have been a good one since breathing was much easier than it had been for a long time but he was unable to sleep This is due to the central stimulation by theophylline which may cause consider

able excitement in some patients Therefore the combination of a sedative with aminophylline is often necessary A barbiturate will usually offset the stimulating effect of aminophylline

Morphine and Sedatives Morphine particularly in the form of an injection of 0 01 Gm or more is contraindicated in Cheyne Stokes breathing In fact even in healthy persons morphine causes Cheyne Stokes which in turn also responds well to aminophylline

A useful sedative for cardiac patients although it has been unjustly avoided for many years is chloral hydrate The doses which depress the circulation are much larger than those customarily employed as a sedative and hypnotic Doses of 2 Gm per rectum or smaller amounts in the form of a syrup by mouth are effective and harmless

CARDIAC ASTHMA AND PULMONARY EDEMA

Cardiac asthma and acute pulmonary edema (paroxysmal nocturnal dyspnea) also result from left ventricular failure and patients presenting these phenomena require digitalis Specific therapy is however necessary during the attacks and in order to prevent recurrences until digitalis brings about the desired effect

Morphine The sovereign remedy in these attacks is morphine If given quickly and in sufficient doses it affords immediate relief While the finer mechanism of its action is still unknown one can assume that it helps by diminishing the excitability of the centers

No stimulating effect of morphine on the circulation is known and morphine certainly does not help to relieve an attack of paroxysmal nocturnal dyspnea by improving the circulation Its prompt effect has always given support to those theories of paroxysmal nocturnal dyspnea which assumed abnormal reflexe or an abnormal condition of the respiratory centers as the causal mechanism

Morphine sulphate is usually given hypodermically during the attack and the dose should not be less than 0 02 Gm Since quick action is necessary and absorption from the cold skin and from the subcutaneous tissue may be slow it is better to administer morphine in this dosage intramuscularly Even the intravenous administration of 0 01 Gm of morphine sulphate has been recommended It is well to include atropine sulphate in the amount of 0 000 , Gm (½ mg) with the injection of morphine

Morphine also prevents recurrences of the attacks Very small doses suffice to guarantee a quiet night and prevent new attacks of cardiac asthma and pulmonary edema An injection of 0 01 Gm of morphine or pantopon or even one tablet or 0 02 Gm of pantopon is given at bed time The most inexpensive method of administration particularly in hospitals is by an aqueous solution of morphine hydrochloride or sulphate The administration of 20—30 drops of a 1 per cent solution usually suffices It has the advantage of rarely causing morphinism at least we have never observed it in many hundreds of cases After a few days the use of morphine usually becomes unnecessary because cardiac action has been improved by digitalis

the consequently increased return of blood to the heart is considered one of the major reasons for the nocturnal appearance of the attacks With the legs dangling the circulating blood volume may be reduced by 400 ml Patients in shock however should lie flat or even with the lower part of the body elevated

Aminophylline Aminophylline has also been recommended for the attacks of cardiac asthma There is no doubt that in the absence of pulmonary edema when expiration is prolonged and difficult when a great deal of bronchospasm exists aminophylline may be useful

Atropine Doses of 1—2 milligrams of atropine have also been recommended for decreasing reflex action and preventing secretion This treatment is useful in experimental pulmonary edema One must however be careful in the intravenous administration of large doses of atropine to patients with coronary sclerosis because the increase of heart rate may cause cardiac hypoxia and may have serious consequences For this reason and owing to the disagreeable side effects of large doses of atropine this treatment is not recommended

Hypertonic Glucose Solution Very effective is an injection of a highly concentrated solution of dextrose for example 40 ml of a 40—50 per cent solution The improvement may appear within a few minutes The action is not ascribed to the sugar A purely osmotic effect of the hypertonic solution is responsible

Intravenous injections of sugar with or without insulin have frequently been recommended for the treatment of various heart ailments These injections were supposed to act particularly well in various myocardial and coronary diseases No proof has been advanced as yet of any beneficial effect The introduction of hypertonic solutions into the circulation causes an appreciable increase of the circulating blood volume by withdrawing fluids from the tissues and augments the load for the heart In patients with cerebral edema an increase of the spinal fluid pressure has been observed after an initial fall Therefore the administration of 50 per cent sucrose has been recommended for these cases The cerebrospinal fluid barrier is not permeable for sucrose Hypertonic solutions of sucrose have however an injurious effect on the kidneys

Even if one employs venesection tourniquets or hypertonic glucose solutions no time should be lost in giving morphine as soon as possible This treatment alone is reliable only in the terminal pulmonary edema is it useless

Morphine in Cardiac and in Pulmonary Dyspnea

It was mentioned in the preceding section that morphine is a most effective remedy for cardiac asthma and pulmonary edema It is no less useful in other forms of cardiac dyspnea

For decades morphine was hailed as a second digitalis and was employed very often in cardiac patients At present its beneficial effects on decompensated and dyspneic cardiac patients is often forgotten

In the chapter on dyspnea it was shown that even the form of breathlessness due to pulmonary congestion does not depend exclusively upon the mechanical

effects of congestion but that various reflexes play an important role In this group of patients examination of the arterial blood reveals no hypoxia As long as no pulmonary complications exist the blood is normally saturated with oxygen and contains even less carbon dioxide than normal blood Pulmonary congestion produces reflex hyperventilation This hyperventilation alone may exhaust the patient because the greater physical work of respiration represents an increased burden It also leads to the detrimental effects of excessive exhalation of carbon dioxide (hypocapnia) If small doses of morphine are given to such patients for instance 20 drops of a 1 per cent solution of morphine sulphate in water and the irritability of the centers is reduced slightly the dyspnea diminishes markedly and with it the added work imposed on the circulation Following one dose of morphine to an otherwise untreated patient one can often observe that in addition to the great subjective relief a profuse diuresis may start and the size of the liver may diminish The great restlessness of these patients is abolished and they can be handled much easier The statement of clinicians about 50 years ago namely that compensation may be achieved with morphine alone is certainly true for some decompensated non fibrillating patients

Therefore every decompensated dyspneic cardiac patient should receive small doses of morphine in the morning and evening for the first few days of treatment until the beginning of the digitalis effect makes this treatment unnecessary The small doses recommended do not inhibit diuresis and no danger of morphinism need be feared if the e doses are given by mouth for the short time they are indicated

At this occasion it is appropriate to stress the fact that in contrast to cardiac dyspnea all types of pulmonary dyspnea contraindicate the use of morphine In these cases oxygen saturation of the blood is diminished and carbon dioxide retention may also take place due to the pulmonary lesion In this instance the *dyspnea is not the abnormal outcome of various factors connected with decom*pensation but an important phenomenon necessary to maintain life and to compensate for the pulmonary lesion Once the irritability of the respiratory centers is reduced by morphine and the respiration is slowed the exchange of gases suffers and hypoxia with increased cyanosis and hypercapnia appear Patients soon fall asleep the breathing becomes more infrequent longer and longer respiratory pauses appear cyanosis increases and soon death may occur by respiratory standstill

This is not a rare event and such occurrences unfortunately are encountered all *too frequently Often* the connection between the administration of morphine and the death of the patient is not clear to the physician he attributes the fatality to the severe pulmonary process It is regrettable that most of the current textbooks of clinical medicine and even of pharmacology do not stress this contraindication

Morphine must be used with greatest care in cases of severe emphysema and kyphoscoliosis in diffuse bronchopneumonia in bronchial asthma in bilateral

tuberculosis and pneumonia, and in diffuse metastatic pulmonary neoplasms. In mild emphysema, bronchopneumonia, tuberculosis or malignancy of the lung, morphine may be administered if indicated; however, in those extensive pulmonary lesions which cause cyanosis or dyspnea morphine is forbidden. We have seen patients die within a half hour with the picture just described because inexperienced physicians ordered morphine for severe pain in a patient with carcinoma and extensive pulmonary metastases or advanced pulmonary tuberculosis. Patients with bronchial asthma rarely die during an untreated attack. This happens, however, often if morphine is given. If for any reason morphine must be administered or the physician is uncertain how much of the dyspnea is of pulmonary origin, small doses of the drug, or, better, demerol may be given. The patient should be watched carefully so that the centrally acting stimulants like atropine, coramine, caffeine or aminophylline can be administered promptly if the depression of the respiration becomes more marked. Nallin in the amount of 5 to 10 mg. is effective.

For the same reason in pulmonary edema, when copious hemorrhagic sputum is already evident and bubbling rales are audible all over the lungs, it is well to omit morphine because a mechanical impediment causes the dyspnea and its suppression may lead to asphyxia. Morphine is given in these cases after one succeeds in causing the absorption of the alveolar transudate by an intravenous injection of hypertonic glucose solution or by the use of a high pressure oxygen mask.

CARDIAC STIMULANTS

In patients with cardiac weakness, preparations of the digitalis or strophanthin group are primarily indicated. In some cases, for instance in acute cardiac failure of various origins, in acute pulmonary edema, in pulmonary embolism and right heart failure, one may find it necessary to stimulate cardiac action immediately before the digitalis glycosides can show an effect on the heart. Sometimes, side effects of digitalis like extrasystoles forbid continuation of digitalis even if it is otherwise indicated. For this purpose, a host of remedies have been recommended but only a few are really useful.

Strychnine. For many years strychnine was employed as a cardiac stimulant. It was early recognized, however, that strychnine has no effect on the heart and can only be used to increase vascular tone. It has been given by mouth or by subcutaneous injection in the dose of 2 mg. three or four times daily.

Pressor Amines. Epinephrine has a very strong action on the circulation. It combines a positive inotropic action on the heart muscle with a constrictor effect on the vessels in wide areas of the body. Nevertheless its disadvantages are great. When given by mouth or by rectum, it is practically inert. If administered hypodermically, its action is sometimes stormy and vanishes in a short time. Even small doses are dangerous to cardiac patients due to the resultant marked tachycardia, the elevation of blood pressure and the remarkable increase of the oxygen requirements of the myocardium which often cannot be

met Therefore this drug should never be used in cardiac patients even if it seems necessary for other purposes for instance as an addition to a local anesthetic or for the treatment of swollen nasal mucous membranes

Some of the newer pressor amines and substances related to adrenalin however are indicated in cases in which for instance in myocardial infarction during local anesthesia or following sympathectomy the blood pressure threatens to fall to dangerously low levels Paredrine and neosynephrine are given in these cases without undue danger to the heart A single dose of 2 mg of paredrine by mouth or 5—10 mg of paredrine or neosynephrine by intramuscular injection may be used Isuprel (10 mg) may be given sublingually

The action of these drugs is more prolonged and less stormy than that of epinephrine

Camphor Coramine Metrazol Preparations of camphor were greatly cherished by many physicians in various countries as cardiac remedies and were given whenever stimulation of the heart seemed indicated There is however no evidence available to prove a stimulating action of camphor on the heart The same holds for some synthetic preparations which were originally recommended as synthetic camphor like stimulants The best known of these preparations are coramine and metrazol (cardiazol) These preparations have no stimulating cardiac effect nor do they increase contractility of the heart They stimulate medullary centers and only in this way lead to a moderate rise of blood pressure and increased respiration They should not be employed for stimulation of the heart muscle

Xanthine Bodies Several preparations belonging to the xanthine group possess a stimulating effect on the heart They are particularly useful because this effect is combined with vasodilatation and some diuretic action

It has been pointed out before that some of the xanthines like theophylline stimulate the heart muscle Caffeine in particular increases the contractility of the myocardium and increases the amplitude of contraction especially of the damaged or weakened heart The effect on the heart rate varies because this depends on various central and peripheral factors which act in opposite directions

For injection the soluble double salts like caffeine and sodium benzoate are used A subcutaneous injection of 0 25—0 3 Gm may be given every two hours when necessary For oral treatment caffeine purum in doses of 0 1 Gm is useful However strong black coffee which the patient may take much more willingly is no less effective than a capsule or an injection of caffeine The caffeine content of a small cup of coffee may exceed the amount given in a capsule or injection

VENESECTION LEECHES

The effect of venesection on cardiac asthma pulmonary edema and in hypertension was discussed in the corresponding chapters This therapeutic procedure is time honored and purely empirical

Patients with marked venous stasis and hepatic engorgement that is patients with right heart failure seem to derive some benefit from phlebotomy

The removal of 400—500 ml of blood may bring relief The venous pressure may fall temporarily and the patient may improve subjectively The *spinal fluid* pressure also falls (Robertson and Fetter) Usually however a delay of several hours is safe and the same result can be secured by an injection of a mercurial diuretic

In patients with right heart failure in the course of pulmonary disease (decompensated cor pulmonale) phlebotomy sometimes affords excellent results In general however this procedure is rarely necessary and rarely used Simultaneously with a lowering of right atrial pressure venesection causes an increase of cardiac output This may be due to the fact that the heart was over loaded before the phlebotomy and the extreme increase of filling pressure had led to a fall in output

It has been pointed out that phlebotomy is helpful in polycythemia complicating pulmonary vascular sclerosis or congenital heart lesions It helps in plethoric patients with chronic congestive heart failure

When the use of leeches is recommended one often encounters a smile of pity We are however able to confirm the observations of others (Sir Thomas Lewis) that this old method of treatment may be very useful if employed upon definite indications The most important situation in which leeches may bring relief is in patients with an acute engorgement of the liver leading to severe pain *in the right hypochondrium* Under these circumstances the application of three or four leeches over the liver suffices to bring relief in a few hours A demonstrable reduction of the size of the liver may be found afterward Although patients object at first to the use of these unpleasant creatures they report definite relief in every instance when the procedure is employed Nothing definite is known about the modus operandi of this measure It has been suggested that the success may be due to the relation of some vascular spasm within the liver via a cutaneous visceral reflex We found however that irritation of the corresponding section of the skin by cantharides plasters or cupping decidedly less effective

Total Thyroidectomy and Other Operations in Cardiac Failure

Total thyroidectomy in patients with intractable angina pectoris has been discussed

It has been known for more than 30 years that subtotal thyroidectomy can exert an excellent effect in patients with organic heart disease and mild hyperthyroidism In these patients the signs of decompensation may vanish soon after the operation sometimes the heart even becomes smaller disturbances *of rhythm* disappear and the functional capacity of the patient increases remarkably The postoperative improvement is very impressive since previously intensive therapy with the most powerful agents available often had failed

The occasional observation of similar striking improvement in patients operated on for an assumed hyperthyroidism although subsequent histologic examination of the thyroid revealed no sign of hyperfunction suggested subtotal

thyroidectomy also for cardiac patients without hyperthyroidism (Blumgart Levine) Since the initial improvement in several cases was followed soon by a recurrence of the original symptoms it was recommended that subtotal thyroidectomy should be discarded and that *total* thyroidectomy be performed The recurrence of symptoms after the older procedure was attributed to regeneration of thyroid tissue

The operation was adopted by many physicians with enthusiasm Others repudiated it At the present time it seems to be rarely employed since thyreoidectomy can be accomplished by drugs without surgery

The procedure deserves consideration in a very carefully observed case if in spite of intensive digitalis therapy the use of the modern diuretics and despite constant hospitalization a tolerable state of compensation cannot be maintained When prolonged observation shows that the myocardium of these patients is in good condition and in the absence of the contraindications to be mentioned presently the operation may be tried One should not treat by thyroidectomy a patient in whom decompensation is merely the result of an infection a pulmonary embolism or an arrhythmia In these instances removal of the cause of decompensation furnishes relief in a simpler way No signs of progression in aortitis should be present and no evidence of activity in cases of rheumatic heart lesion

At first the success of the procedure was ascribed to the fall of the basal metabolic rate It was believed that the operation leads to a diminished oxygen requirement in the tissues and thus the demands of the tissues are adapted to the impaired circulation But it soon became clear that the improvement appears before the basal metabolism is lowered indeed occasionally it was evident a few days following the operation Therefore abolition of a direct thyroid effect on the circulation is involved When the basal metabolic rate falls to low levels and evidence of hypothyroidism appears small doses of thyroid are given Sometimes we were able to maintain the basal metabolic rate at a normal level in these patients while the improvement of the circulation remained

One must also consider that fact that with the development of myxedema the cardiac output as well as circulation time fall to lower levels This too forces us to seek for another explanation for the benefit of surgical or chemical thyroidectomy than simply the diminution of the oxygen requirements of the tissues

Another indication for this mode of therapy are patients with paroxysmal tachycardia or paroxysmal flutter and fibrillation who suffer from very frequent attacks and who do not respond to the usual therapy Here diminution of thyroid activity may lessen the severity and incidence of the attacks

Thiourea derivatives proved helpful and were used with advantage in patients with congestive heart failure as well as in patients with angina pectoris However the simplest and for the patient least inconvenient therapy is that with radioiodine The iodine uptake is at first determined with a tracer dose of I^{131} Then doses of 20—30 millicuries are given orally in intervals of 5—6 weeks Often good results are obtained early after the first dose The development of a myxedematous state is by no means necessary

It is claimed that in congestive cardiac failure this therapy helps in about 50 per cent of the cases In angina pectoris excellent results were reported in one third of the cases and worthwhile results in another one third In the latter group we found chemical thyroidectomy particularly helpful in patients with aortic stenosis and aortic insufficiency and decubital angina Recently Blumgart et al reported worthwhile improvement in 75 per cent of patients with angina pectoris and about 60 per cent of patients with congestive heart failure

Other Operations in Congestive Heart Failure

In patients with congestive cardiac failure particularly in mitral lesions Cossio recommended ligation of the inferior vena cava Satisfactory results were reported by him and others (Bernath et al) The operation is contraindicated in high output failure but provided immediate relief in the congestive heart failure of mitral patients

These operations as well as the creation of an artificial experimental tricuspid insufficiency (Cossio et al) are now superseded by direct operation on the cardiac valves

ANTICOAGULANTS IN CONGESTIVE HEART FAILURE

Thromboembolism in patients with congestive heart failure is a common complication and about one third of patients with rheumatic valvular lesions develop heart failure because of pulmonary emboli If — as usually happens — the patient is forced to stay in bed the danger of new embolism is even greater

The thrombi are not only located in the lower extremities but also and even more extensively in the venous plexusses of the pelvis the hypogastric veins the prostatic and ovarian plexusses which we had examined for years in every post mortem examination of patients dying from congestive heart failure and which we found thrombosed in practically every instance

Such pulmonary embolisms coming repeatedly over a prolonged period may by themselves cause heart failure and are detrimental for patients whose hearts are already overburdened because of rheumatic fever or coronary sclerosis

It has often been stated that therapy with digitalis increases the danger of thrombus formation In a careful study of this question Cormsen found no correlation with the degree of diuresis and thrombosis but a good correlation between intensity of therapy and thrombosis

For these reasons prolonged anti coagulant therapy has been recommended in patients with congestive heart failure (Wishart and Chapman Harvey and Finch) and a significant r duction of the occurrence of thromboembolism has been reported Griffith et al found in the treated group an incidence of thi complication of 1 8 per cent while it was 15 5 per cent in the untreated group

A final deci ion on whether or not the measure should be u ed routinely is not yet pos ible One will understand that by the use of anticoagulants new hazards are added to those already existing It should app ar advisable to wait until

studies covering a large amount of material show that the dangers of the therapy are minor and the advantages outweigh them

DIETARY QUESTIONS

Even if no special diet is required detailed instructions should be given to cardiac patients since the definite advice is always welcome

Compensated cardiac patients in general need not be subjected to great dietary restrictions A normal mixed diet is permissible Foodstuffs which cause flatulence foods which are not easily digested and large meals should be avoided Eat frequently but do not take too much at one time is an excellent precept Fluids should be taken mainly between meals

The dietary requirements in patients with hypertension coronary sclerosis or myocardial infarction have been discussed in the chapters dealing with these conditions

Patients with cardiac failure and edema should receive a diet poor in salt or even salt free Even healthy persons who receive a salt free diet for one day have a profuse diuresis and show a loss of weight surpassing 1 Kg within 24 hours The great contribution of such a diet to the development of a satisfactory diuresis in edematous patients is readily understandable

Pecently a high fluid intake has been recommended in cardiac edema (Schemm) It was pointed out that edematous patients may even be dehydrated If the sodium in the diet is restricted and the diet yields a neutral or acid ash remarkable diuresis may be obtained even with administration of more than 4 000 ml of water daily Meat eggs cereal prunes and plums belong to the food stuffs giving an acid ash Milk fruit juices and fruit with the exception of those mentioned above should be avoided Ammonium chloride (3 Gm daily) or a few drops of dilute hydrochloric acid in every glass of water serve to increase the acidity This diet has been abandoned by us and in many other places

The Karell diet consisting of 800—1 000 ml of milk only taken during the day is very satisfactory The use of milk has however some disadvantages Many patients do not like it in many it causes meteorism and distension and in others diarrhea Moreover milk is salt poor and not salt free It contains 750 mg of sodium per liter For this reason raw or cooked vegetables may be substituted for milk All varieties of fruits or vegetables are permissible Even potatoes are allowed particularly for heavy eaters They may be eaten with the skin which on account of their high content of potassium are supposed to exert some diuretic effect The total quantity of fruit or vegetables permitted during 24 hours should not exceed 1 200 Gm No other food and no other drinks are given This diet is followed for three days in succession and then supplemented by proteins

Artificial salts have been devised but most of them have a high content of sodium and are therefore of little value Usually one can dispense with them Garlic pepper paprika vinegar and the like are permitted

In patients who develop marked albuminuria a hypoproteinemia may appear during chronic congestion Therefore a diet rich in proteins is necessary

In patients who are overweight a low caloric intake will be prescribed For most patient 20 calories for one Kg body weight are suggested The calculated ideal weight of the patient rather than the actual weight should serve as a basis for the dietary regime

The amount of liquid permitted to a patient with decompensation should not exceed 800—1 000 ml within 24 hours Naturally fruits vegetables soups are calculated as fluids

Excessive smoking and consumption of large quantities of alcohol are prohibited It has been stressed in the appropriate chapters that in patients with hypertension with coronary diseases and particularly in patients with peripheral vascular diseases smoking is harmful even in smallest quantities while alcohol taken in moderation is useful

AIR TRAVEL CLIMATE

In this era of air travel the question must often be decided whether the patient may undertake a trip by plane With the exception of obvious contraindications such as severe congestive heart failure or a fresh myocardial infarction the answer will most often be yes The small risk is illustrated by the experience (Graybiel) that among 7 million passengers carried by five major airlines only 3 deaths occurred during flight and 5 shortly after landing from cardiovascular disease The rule if you can walk you can fly was accepted but consideration should be given to certain facts

A patient with a myocardial infarction should not fly until four months have elapsed since the day the infarction occurred Dyspneic patients should not fly Among laymen the opinion prevails that pressurized planes are safe however they are pressurized at a level of 7 000—8 000 feet Some patients with angina pectoris need oxygen at 5 000 feet Patients with status anginosus or attacks of angina pectoris at rest (angina de decubitus) should not fly Abdominal distention due to the expansion of abdominal gases often causes discomfort The administration of 1 tablet of dramamine every four hours is recommended

Cardiac patients particularly those with congestive heart failure do not tolerate humid and hot climate well On the other hand even in a subtropical climate patients with angina on effort are more comfortable and the need for nitroglycerin diminishes

The literature on observations on the occurrence of attacks of coronary thrombosis or apoplexy in connection with particular barometric pressures and other climatic factors is large In Dallas Texas the incidence of myocardial infarction during the summer months is greater (Heyer et al) while the incidence in Northern cities seems to be greater in the winter Others reached different conclusions (Schnur) A sudden elevation of atmospheric temperature and humidity may precipitate an attack of left ventricular failure

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